

MINIMAL CHANGE DISEASE, THE LEADING CAUSE OF GLOMERULOPATHIES IN PAEDIATRIC POPULATION AT PESHAWAR

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Background: Glomerulonephritis (GN) is a relatively rare disease with numerous subtypes. Most regional nephrology centres see only a limited number of patients with each type of GN every year. The objective of this study was to find out the pattern of glomerulopathies in paediatric population, undergoing renal biopsy in Peshawar. **Methods:** This was a prospective study carried out at the Department of Nephrology, Khyber Teaching Hospital, Peshawar from May 2002 to May 2004. Ultrasound guided percutaneous renal biopsies were carried out in patients with the findings of: 1) Nephrotic range proteinuria in children, 2) Non-nephrotic range proteinuria with evidence of hypertension/haematuria/deranged renal function or active sediments on urine microscopy, 3) Steroid resistant nephrotic syndrome in children, and 4) Children with nephrotic syndrome who were not tolerant of steroid therapy or were considered for immunosuppressive drugs. **Results:** A total of 155 renal biopsies were taken. Out of these 90 were male patients and 65 were female. The most common histopathological lesion among children population was Minimal Change Disease (42.66%) followed by Focal Segmental Glomerulosclerosis (25.33%) and Membranous Glomerulonephritis (16.0%). Nephrotic range proteinuria was most prevalent in Minimal Change Disease and Membranous Glomerulonephritis followed by Focal Segmental Glomerulosclerosis. Non-nephrotic range proteinuria was mostly seen in patients with Membranoproliferative Glomerulonephritis. **Conclusion:** In paediatric population, Minimal Change Disease is the most commonly encountered glomerulopathy, followed by Focal Segmental Glomerulosclerosis and Membranous Glomerulonephritis.

Keywords: Nephrotic Syndrome, Renal biopsy, Proteinuria, Glomerulopathy

INTRODUCTION

Glomerulonephritis (GN) is a relatively rare disease with numerous subtypes. Most regional nephrology centres see only a limited number of patients with each type of GN every year. Information about the prevalence and incidence of GN in the general population is rather scarce; comprehensive epidemiological surveys are difficult to undertake, especially since the onset of most cases of GN is 'silent' so the diagnosis is often incidental, made by urine testing during a routine medical examination.¹

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.²

Percutaneous biopsy needle from Menghini needle, Vim Silvermann and its Franklin modification (Trucut), to automated spring loaded gun have increased the yield of successful biopsies from 60% to 90% with minimal associated complications.³

Percutaneous renal biopsy (PRB) was introduced in early 1950s and since then, with the advancement of imaging technique and biopsy needles, the procedure has been simplified with improved success rate. Now a days the PRB is a

relatively safe procedure with life threatening complications occurring in <0.1% of biopsies¹⁻⁴ and diagnostic yield of >96%.¹

Recently there has been a major shift towards utilisation of spring-loaded disposable gun devices. In addition to percutaneous and open renal biopsy, transjugular and even laparoscopic renal biopsies are being carried, where indicated.

Renal biopsy is indicated in patients with renal disease when all the following 3 conditions are met:

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

The standard of care after renal biopsy includes close observation and bed rest for 24 hours following the procedure. With ever increasing safety profile of renal biopsy, in selected group of patients the procedure can be performed on out-patients basis by experienced nephrologists and patients can be discharged only after 6 to 8 hours of observation.⁵⁻⁷

MATERIAL AND METHODS

This retrospective study was carried out in the Department of Nephrology, Khyber Teaching Hospital Peshawar, over a period of 2 years (May

2002 till May 2004). A total of 155 renal biopsies were performed during this period in children population. To determine the frequency of different glomerulopathies in paediatric population (age less than 12 years) having significant proteinuria due to renal diseases. Strict inclusion and exclusion criteria were used as per following details:

Inclusion criteria

1. Nephrotic range proteinuria in children.
2. Non-nephrotic range proteinuria with evidence of hypertension/haematuria/deranged renal function or active sediments on urine microscopy.
3. Steroid resistant nephrotic syndrome in children (patients not responding to steroid in eight weeks time).
4. Children with nephrotic syndrome who were not tolerant of steroid therapy or were considered for immunosuppressive drugs

Exclusion criteria

1. Age more than 12 yrs.
2. Known diabetics with proteinuria (more than 5 year duration).
3. Bilateral small echogenic or scared kidneys.
4. Polycystic kidney and congenital nephritis.
5. Typical history of preceding throat infection followed by active sediment in urine microscopy.
6. Sudden onset of simple proteinuria with normal renal functions and normal Blood pressure.

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

Real time ultrasound guided renal biopsies were done. Spring-loaded disposable percutaneous biopsy needle was used in all the patients (18G for children).

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

RESULTS

A total of 155 renal biopsies, were performed during this study. Out of these, 90 (58.0%) were male and 65 (41.9%) were female. The mean age of the patients in our study was 6.75±4.14 years with a range of 8 months to 12 years. The average duration of illness in this series was 3.7 months (ranging from 15 days to 8 months).

A total of 150 out of 155 renal biopsies (96.77%) fulfilled the inclusion criteria of the study. The commonest indication for biopsy was proteinuria

alone accounting for 106 (70.66%) cases. The next commonest cause was proteinuria with haematuria in 17 (11.33%) cases, followed by proteinuria with deranged renal function in 10 (6.66%) cases, unexplained acute renal failure in 9 (6.0%) cases, and haematuria alone/with deranged renal function accounting for 8 (5.33%) cases.

The histopathological findings among the biopsied patients in the age group of less than 12 yrs showed that Minimal Change Disease (MCD) was the most frequently occurring entity accounting for 64 (42.66%) cases, followed by Focal Segmental Glomerulosclerosis (FSGS) and Membranous Glomerulonephritis accounting for 38 (25.33%) cases and 24 (16.0%) cases respectively (Table-1). The remaining glomerulopathies were Mesangio-proliferative Glomerulonephritis (MPGN), Tubulo Interstitial Nephritis (TIN) and Acute Tubular Necrosis (ATN) each having 8 (5.33%) cases.

The associated conditions, which we encountered with different glomerulopathies in this series, are summarised in Table-2. Five patients had Hepatitis B positive status, while 6 patients were having Upper Respiratory Tract Infection (URTI). One patient with Ventricular Septal Defect (VSD) was detected.

Table-1: Proteinuria in Glomerulopathies

Glomerulopathy	Proteinuria (>3 gm/day) n (%)
Minimal Change Disease	64 (100%)
Membranous Glomerulonephritis	24 (100%)
Focal Segmental Glomerulosclerosis	26 (68%)
Acute Tubular Nephritis	4 (50%)
Tubulointerstitial Nephritis	4 (50%)
Membranoproliferative Glomerulonephritis	3 (37.5%)

Table-2: Associated conditions in Glomerulopathies

Type of Glomerulonephritis	HBs Ag Positive	URTIs	VSD	Total
Post. Infective Glomerulonephritis		5		5
Membranous Glomerulonephritis	4			4
Minimal Change Disease	1		1	2
Focal Segmental Glomerulosclerosis		1		1
TOTAL	5	6	1	12

DISCUSSION

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

The most common histopathological lesion in paediatric population (age<12 yr) in our series is Minimal Change Disease (MCD), Focal Segmental Glomerulosclerosis and Membranous Glomerulonephritis. This is comparable to that reported by Farida and Azhar⁸ and Noor Khan *et al*⁹. According to Hafeez

and Rasool, Mesangioproliferative Glomerulonephritis is the leading entity followed by Membranoproliferative Glomerulonephritis and Minimal Change Disease.¹⁰ This is probably because they also included the children who were suspected of post-infective GN in their study. Histological examination of biopsies at Mayo Hospital Lahore revealed focal segmental glomerulo-sclerosis in 12 (27.9%), minimal change disease in 9 (20.93%), membranoproliferative/mesangiocapillary glomerulonephritis in 7 (16.27%), mesangial proliferation in 4 (9.30%), and membranous nephropathy in 2 (4.65%) cases.¹¹ Two landmark studies from our Asian region also confirmed the finding of MCD as the leading cause of proteinuria in paediatric population. A large study carried out in Malaysia showed that in more than 2,000 paediatric population, MCD and Membranous GN were the leading entities in that group of patients.¹²

Similarly, in a prospective study showing the pattern of glomerulonephritis in Singapore children, of the primary Glomerulonephritis, MCD was the most common (22%) followed by focal global sclerosis (20%), focal segmental glomerulosclerosis (17%), and diffuse mesangioproliferative Glomerulonephritis (11%).¹³

Regarding the presence of nephrotic range proteinuria versus non-nephrotic range proteinuria, the earlier finding at Rawalpindi by Yaqoob *et al*¹⁴ that Membranoproliferative Glomerulonephritis is the leading cause of non-nephrotic range proteinuria and Membranous Glomerulonephritis the leading cause of nephrotic range proteinuria, was also validated by similar findings in our study. It is seen that Minimal Change Disease and Membranous Glomerulonephritis are the commonest entity with proteinuria of more than 3 gm/day, followed by Focal Segmental Glomerulosclerosis and Membranoproliferative Glomerulonephritis, (Table-2).

More importantly the finding of deranged renal function with different glomerulopathies, we observed that both Membranous Glomerulonephritis and Minimal Change Disease are rarely associated with significant renal impairment.

We did not find any significant number of Mesangioproliferative Glomerulonephritis in this series because all those cases suspected of having post infective GN were excluded from our study. Similarly we could not show any IgA nephropathy due to the lack of Immunofluorescence studies of 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 Glomerulonephritis.

As different studies have shown, the risk of complications significantly reduces when biopsy is carried out by an expert person.¹⁵ This was also confirmed in this series, as our team encountered no major complications during the study period.

CONCLUSION

In children, Minimal Change Disease is the most frequently encountered glomerulopathy followed by FSGS and Membranous Glomerulonephritis. Percutaneous renal biopsy is a safe procedure in expert hands with minimal complication. It helps the nephrologist to find out the underlying histopathology for proper diagnosis and better management.

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