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Histopathological pattern of pediatric renal disease – our experience at Kamineni Hospitals, Hyderabad

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Abstract

Introduction: Renal biopsies are very important in diagnosing and managing children with renal diseases. There are few studies which highlight the histological pattern of renal diseases in pediatric age group.

Objective: This study was conducted to analyse indications for renal biopsies, and also histological pattern of renal diseases in children which were referred to the Pathology department, Kamineni Hospitals, Hyderabad by the Nephrology department, Government General Hospital, Kurnool.

Materials and Method: A retrospective analysis of kidney biopsy reports from December 2013 to December 2016 was done. Adult biopsies, inadequate and renal allograft biopsies were excluded from the study. Only pediatric age group of 1-14 years was considered.

Results: Out of total 750 biopsies, 130 cases belong to pediatric age group. Male to female ratio is 1.8:1, with a mean age of 10 + of -4. Nephrotic syndrome is the most common indication for renal biopsies and histologically minimal change disease (MCD) is the most common (43%) histological pattern followed by membranoproliferative glomerulonephritis (MPGN) (18%), focal segmental glomerulosclerosis (FSGS) (11%), and Post infectious glomerulonephritis PIGN (10%) etc.

Conclusion: Nephrotic syndrome is the most common indication for renal biopsies and MCD is the most common type of glomerulonephritis among pediatric cases diagnosed at our institution.

Introduction

Renal biopsies are very important in diagnosing and managing children with renal diseases. Indications for renal biopsies vary from center to center.(1) The common clinical indications for renal biopsy include nephrotic syndrome (NS), prolonged acute renal failure (ARF), rapidly progressive renal failure (RPRF), systemic disease with renal dysfunction, non-nephrotic proteinuria, isolated microscopic hematuria, unexplained renal failure, renal transplant dysfunction, and familial renal disease.(2) Renal biopsy is less frequently performed in children compared to adults. This difference is due to the fact that the nephrotic syndrome in children is assumed to have minimal change disease (MCD), and steroid therapy is given without going for biopsy as it is invasive and painful.(3,4) Now with the availability of automated triggered biopsy gun, and real time ultra sound, kidney biopsy is a safe procedure that can be easily performed.

There are several published reports on pediatric kidney biopsies from different countries. In India, very few reports have been published giving insight into epidemiological data and the spectrum of clinically significant renal disease. Immune mechanisms are responsible for glomerular injury in majority of cases of primary glomerulonephritis (GN), and many of the secondary GN. Correct diagnosis of glomerulonephritis requires renal biopsy and histopathological examination by light microscopy, immunofluorescence and electron microscopic examination. Facilities for electron microscopic studies are not easily available in India. In most cases, light microscopy (LM) and direct immunofluorescence (DIF) studies are adequate for definite diagnosis of GN.(5) Patients with immune deposits can be treated easily with steroids or immunosuppressants. We conducted this study to analyse indications for renal biopsies and their histological pattern in pediatric cases.

Materials and Method

A retrospective analysis of kidney biopsy reports from December 2013 to December 2016 was done. All biopsies were done at Government General Hospital, Kurnool, Andhra Pradesh, and were transported to Kamineni Hospitals, Hyderabad in Michels Media for DIF, and in formalin for LM. The age group considered was 1-14 years. Renal biopsies of adult patients, inadequate and renal allograft biopsies were excluded from the study.

Minimum workup of the patients included clinical presentation (Nephritic/Nephrotic/End stage disease/others), size of the kidneys, blood pressure, blood urea, serum creatinine, and urine analysis giving albumin and sugar levels and microscopy, including red blood cells, white blood cells per high power field and casts.

All biopsies were performed by a well experienced nephrologist using an automatic triggered biopsy gun. Histopathological evaluation of the biopsy specimens was done by LM and DIF. Electron microscopy was not available. In Light Microscopy, biopsies were stained routinely with Hematoxylin and Eosin (Fig. 1a, 1b, & 1c), Periodic acid schiff stain (Fig. 1d), Masson Trichrome stain, and Silver methenamine. Direct

Immunoflourescence staining was done with antibodies against Immunoglobulins A, G, M, and C3c, and C1q. All specimens were reviewed by two qualified pathologists. The data were stored in Microsoft excel and statistics like percentage, and mean were calculated.

Results

A total of 750 renal biopsies were analysed, out of which 130 cases belonged to pediatric age group. Male to female ratio was 1.8:1, with a mean age of 10 + 4.

The most common indication for renal biopsy was nephrotic syndrome: 100 (77%) followed by nephritic syndrome: 14 (10.7%), Rapidly progressive renal failure (RPRF): 6(4.6%), Lupus nephritis: 8(6.4%), and Acute glomerulonephritis (AGN): 2(1.5%) [Table 1]

Table 1: Pattern of Clinical Indications for Renal biopsies in Children

Clinical Indication for Biopsy	Numbers (%)
Nephrotic Syndrome(NS) ?MCD/FSGS/MGN/MPGN	80 (61.5)
Steroid Dependent NS	18 (13.8)
Steroid Resistant NS	02 (01.5)
Nephritic Syndrome	
Crescentic Glomerulonephritis	02 (01.5)
?IgA Nephropathy	12 (09.2)
Rapidly Progressive Renal failure	06 (04.6)
Acute Glomerulonephritis	02 (01.5)
Lupus Nephritis	08 (06.4)
Total	130 (100.0)

MCD-minimal change disease, FSGS-focal segmental gomerulo sclerosis, MGN-membranous glomerulo nephritis, MPGN- membranoproliferative glomerulo nephritis.

Minimal change disease (MCD) is the most common (43%) histological pattern followed by membranoproliferative glomerulonephritis (MPGN) (18%), focal segmental glomerulosclerosis (FSGS) (11%), and Postinfectious glomerulonephritis PIGN (10%) etc. [Table 2]

Table 2: Histopathological pattern of Renal diseases in Children

S. No	Histopathological patterns of Renal disease	1-10 years		11-14 years		Number (%)
		Male	Female	Male	Female	
1	Minimal Change Disease	22	13	16	05	56 (43)
2	Membranoproliferative GN	06	03	10	04	23 (18)
3	FSGS	03	02	09	00	14 (11)
4	Post infectious GN	03	01	06	03	13 (10)
5	Membranous GN	00	00	01	04	05 (4)
7	IgA GN	00	00	04	00	04 (3)
8	Crescentic GN	00	00	01	02	03 (2)
8	Lupus Nephritis	01	00	00	04	05 (4)
9	Ac TI nephritis	00	00	01	04	05 (4)
10	Non specific	00	00	01	01	02 (1)
	Total	35	19	49	27	130 (100)

GN: Glomerulonephritis, FSGS: Focal Segmental glomerulosclerosis, Ac TI nephritis: Acute tubulointerstitial nephritis

Discussion

This study provides information about the clinical indications for renal biopsies and histopathological patterns of renal disease in children diagnosed during the study period at our institute. A total of 130 cases were studied, and male: female ratio was 1.8:1. Of these 100 cases (76.8%) were children with nephrotic syndrome.

In the present study the most common indication for renal biopsy was nephrotic syndrome, and the most common histopathological pattern, irrespective of age and gender groups, observed was minimal change disease (MCD) followed by membranoproliferative glomerulonephritis (MPGN), Focal segmental glomerulosclerosis (FSGS), Postinfectious glomerulonephritis (PIGN) and membranous glomerulonephritis (MGN).

The underlying etiology of NS is variable across the globe. Results from the other retrospective studies from other geographical regions are presented in Table 3. The three most common histopathological patterns in NS are to be MCD, FSGS, and MPGN, with slight variation in their order.[6-14] Our study is consistent with other regional studies of pediatric age group.

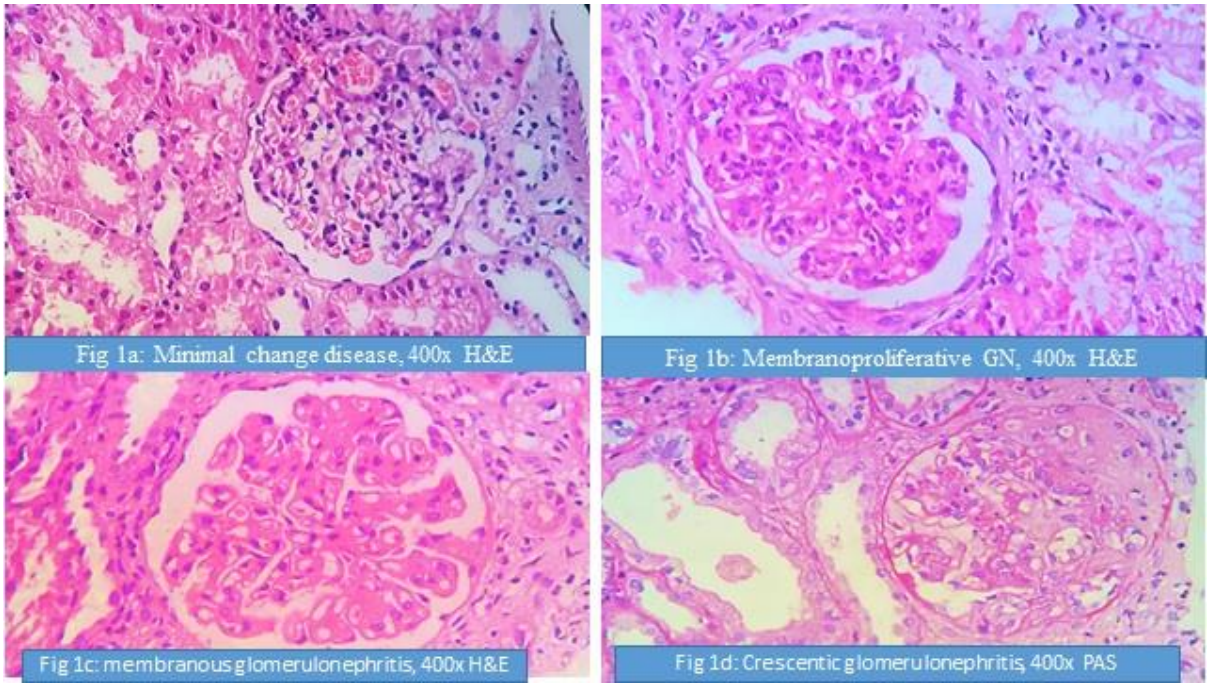

Table 3: Most common clinical indications for renal biopsies in children and most common histopathological patterns from different countries

S. No	Most Common Indication	Most common Histopathological pattern	Country
1	Nephrotic Syndrome (NS)	MPGN	Turkey[6]
2	NS	MCD	Iran[7]
3	NS	MCD	India[8]
4	NS	FSGS	India[9]
5	NS	FSGS	USA[10]
6	NS	MCD	Pakistan[11]
7	NS	MCD	Korea[12]
8	NS	MCD	Italy[13]
9	NS	MPGN	Croatia[14]
10	NS	MCD	Present study

MPGN: Membranoproliferative glomerulo nephritis, MCD: Mininmal change disease, FSGS: Focal segmental glomerulo sclerosis

Combined analysis of both light microscopy and DIF are required for correct diagnosis.

Minimal change disease is the most common histological pattern (Fig. 1a) in correlation with immunofluorescence (IF) findings similar to other studies.[8,9,12-14] In MCD, histologically we found absolutely normal looking glomeruli, with no evidence of endocapillary proliferation, no increase in mesangial matrix or cellularity. No crescents/sclerosis/necrosis were observed. IF wise nil findings were noted.

In the present study minimal change disease was more common in boys than girls, with a ratio of 2.1:1, similar to white RH et al.[15]

Membranoproliferative glomerulonephritis is the second most common diagnosis in the present study, wherein histologically we identified characteristic glomerular findings like diffuse involvement, marked endocapillary proliferation with thickened glomerular basement membrane, and lobular accentuation, increased mesangial matrix with cellularity, and leukocytic inflammation. (Fig. 1b), IF findings showed granular deposits of both IgG, C3c along the GBM and mesangium.

In certain cases of FSGS, the initial histological pattern resembles MCD, presence of IgM antibodies in the mesangium, in focal segmental pattern will distinguish it from MCD. It shows the significance of IF. Other situation like membranous glomerulonephritis stage -1, we did not find thickening of capillary basement membrane, and no spikes on silver methenamine stain and it was very difficult to distinguish it from minimal change disease. Here comes the role of IF, which helps in diagnosing the correct entity.[16]

Kumar J et al.,[17] in their study observed that the age at onset of NS was significantly higher in the non-MCD group than MCD group, and MCD is the most common histological pattern seen under 8 years, and FSGS is the most common histological pattern seen after 8 years. In the present study irrespective of age and gender groups the most common histological pattern was minimal change disease (MCD) with nephrotic syndrome.

Due to lack of EM facilities, cases like Alport syndrome, and thin basement membrane nephropathy could not be diagnosed conclusively in the present study.

Membranous glomerulonephritis (MGN [Fig. 2a]) has been reported less frequently in the children,[18] similarly in the present study MGN was not reported in children with below 10 years, and only 4% cases were noted in children between 11 -14 years.

Among secondary glomerulonephritis, lupus nephritis was seen more with females (3%) compared to male (<1%) in the present study, similar to other regional studies.[19,20]

Tubulo-interstitial nephritis is very uncommon in children,[19] only 4% cases were noted in the present study.

From South India, Das U et al.,[21] studied pattern of biopsy proven renal disease in adult population with mean age of 32 + 18 years. The most common indication for biopsy and common histological pattern observed were similar to the present study. But in the study by Chandrika BK,[22] the most common histological pattern was focal segmental sclerosis, and in the study done by Rahul Mannan et al.,[23] the most common histological pattern was membranous glomerulonephritis, though the NS was the common indication for biopsy.

We recommend renal biopsies in all pediatric cases as it is very safe and easy to perform. Biopsy will give correct diagnosis and appropriate therapy in the sense right doses of steroids or other immunosuppressive drugs will be given as per the guidelines published by the Indian Pediatric Nephrology Group.[24]

Conclusion

Nephrotic syndrome is the most common indication for renal biopsy and the histological pattern observed may vary with age and geographic distribution. Minimal change disease was the most common histological pattern observed in the present study.

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