

Pattern of Renal Histopathological Findings in Children: A Single Center Study

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ABSTRACT

Introduction: A well-known diagnostic tool for determining kidney diseases in paediatrics is renal biopsy. It aids in selection of precise therapeutic approaches for several renal diseases.

Aim: To explore the indications and histopathological patterns of renal diseases in children in a tertiary care center in Odisha, India.

Materials and Methods: A retrospective study involving renal biopsies were performed on children aged ≤ 14 years between January 2010 and July 2018. All renal biopsies were studied under light and immunofluorescent microscopy. The clinical characteristics and histological diagnosis pertaining to each case during the study period were retrieved from medical records and analysed.

Results: A total of 443 biopsies were considered for analysis. The mean age was 5.94 years (range 4 months-14 years) with a predominance of boys (62.97%). The most common indication

for renal biopsy was Nephrotic Syndrome (NS) (79.9%) followed by lupus nephritis (5.19%), Acute Kidney Injury (AKI) (3.16%) and haematuria (2.25%). Steroid Dependent Nephrotic Syndrome (SDNS) was the most frequent indication among all NS children. Minimal Change Disease (MCD) was the most common histopathological finding in NS which constituted 47.63% followed by Focal Segmental Glomerulosclerosis (FSGS) 22.12%. The biopsy report of the children with lupus nephritis showed the disease progression to stage IV. Most common primary glomerulonephritis was MCD while secondary glomerulonephritis was lupus nephritis.

Conclusion: MCD was the most common histological finding. The present study provides largest data on Biopsy Proven Renal Disease (BPRD) in children from eastern India published till date.

Keywords: Biopsy, Glomerulonephritis, Immunofluorescent, Kidney, Lupus nephritis, Nephrotic syndrome

INTRODUCTION

Kidney diseases including Chronic Kidney Disease (CKD) and End Stage Kidney Disease (ESKD) is a major concern globally in adult and paediatric population [1]. The manifestation of kidney diseases in India lacks data collection at national and local level due to dearth of resources, unawareness among the general public, hence the factual number of cases is underestimated [2]. Developed countries have advanced screening techniques to detect kidney diseases whereas developing and underdeveloped countries lack epidemiological data of kidney diseases due to scarcity of resources [3]. Hence, careful evaluation is needed in these population who cannot afford expensive treatment cost and renal replacement.

Clinical and histopathological knowledge obtained from various diagnostic means can help in early detection of renal diseases ensuing reduced morbidity and mortality of patients. Numerous diagnostic modalities are available that are non-invasive like urine or plasma biomarker analysis and invasive methods like renal biopsy [4].

Renal biopsy is a process of extracting a renal tissue by means of renal needle (percutaneous renal biopsy) or surgically (open biopsy). It is an invaluable means for early diagnosis and management of renal diseases [5]. It is a guide to determine the disease progression and helps shaping up the medication therapy. The biopsy data can be useful in directing the course of treatment, avoid toxic therapies in impaired renal conditions and reduce complications. Renal biopsy is indicated in several diseases with renal involvement.

Major complications occurring after the biopsy are incidences of bleeding, infection, haematuria, haematoma, bladder obstruction and occasionally death [5]. In few conditions, renal biopsy cannot be opted such as presence of cysts or renal tumors [6], atrophic kidneys or horseshoe kidney, hypertensive or hypotensive patients, renal abscesses, pyelonephritis, severe anaemia and uremia, however, some conditions if treated in advance like anaemia, uremia or urinary obstruction, then biopsy can be done without harm [7]. Biopsy is broadly indicated in conditions like acute or

rapidly progressive renal failure, NS, non-nephrotic proteinuria, Acute Kidney Injury (AKI), CKD, persistent glomerular haematuria, systemic diseases with renal involvement [8,9]. There are generally two types of renal biopsies; targeted and non-targeted wherein targeted is more preferred by the nephrologist due to its accuracy, specificity and high prognostic value [10,11].

Furthermore, patients with similar clinical symptoms exhibit misleading clinical and pathological findings causing incorrect prognosis. In such cases, renal biopsy is an ideal diagnostic procedure but its safety in paediatric patients has been a concern. However, advancement in technology of renal biopsy has led to innovation of safe and reliable diagnostic means to detect associated renal problems in pediatrics [12-14].

The present retrospective study reports the clinical indications and histopathological patterns of renal diseases in children and determines the factors affecting the diagnosis.

MATERIALS AND METHODS

This was a retrospective study conducted at the Department of Paediatrics, SVP Post Graduate Institute of Paediatrics (SVPPGIP) and SCB Medical College, Cuttack, Odisha, India. The study protocol was approved by Institutional Ethics Committee. All renal biopsies performed in children aged ≤ 14 years between January 2010 and July 2018 at the center were considered eligible and were included in the study. All renal biopsies were studied under light and immunofluorescent microscopy. The medical records of included patients were reviewed and biopsy gun details, clinical characteristics and histological data were noted. One biopsy sample was considered adequate to include patient in the study.

NS was defined if urinary protein >1 g/m² per 24-hour, serum albumin <25 g/L, serum cholesterol >250 mg/dL [6], and generalised oedema. Steroid dependence was defined as relapse within 14 days withdrawal of steroids and requirement of steroids to maintain the remission. The numbers and percentages of causes related to each clinical indication and histopathological findings were identified and

analysed. Children with two coexistent glomerular diseases and those displaying less than 10 glomeruli for light microscopy where possibility of precise diagnosis by immunofluorescence or electron microscopy was so were excluded from the study.

RESULTS

A total of 443 biopsies were performed in children aged less than 14 years during the study period and were considered for analysis. Of the 443 cases, 279 (62.97%) were boys and 164 (37.03%) were girls. The mean age was 5.94 years and the age ranged from 4 months to 14 years.

The most common indications for renal biopsy was NS (79.91%) followed by lupus nephritis (5.19%), AKI (3.16%), nephro-nephritic syndrome (2.93%), acute glomerulonephritis (2.70%) and haematuria (2.25%) with few other indications as listed in [Table/Fig-1]. SDNS was the most common indication among all the children with NS. MCD was the most common histopathological finding in NS and constituted 47.63% patients followed by FSGS 22.12% followed by IgA nephropathy (4.96%) and IgM Nephropathy (4.06%) [Table/Fig-2]. Stage IV lupus nephritis was the most common biopsy findings in children with lupus nephritis (2.71%) followed by stage III (1.35%). The most common primary glomerulonephritis was MCD while secondary glomerulonephritis was lupus nephritis.

Indication	Number of patients (n=443)
Nephrotic syndrome	354 (79.91)
Lupus nephritis	23 (5.19)
Acute kidney injury	14 (3.16)
Nephro-nephritic syndrome	13 (2.93)
Acute glomerulonephritis	12 (2.70)
Haematuria	10 (2.25)
Chronic kidney disease	7 (1.58)
HSP nephritis	5 (1.12)
HUS	3 (0.67)
Malarial nephropathy	1 (0.22)
Renal transplant	1 (0.22)

[Table/Fig-1]: Summary of biopsy indications.

Data shown as n (%), unless otherwise specified;

HSP: Henoch-Schönlein purpura; HUS: Hemolytic uremic syndrome

DISCUSSION

Renal biopsy is a useful diagnostic tool preferred by many nephrologists especially when all other tests tend to fail or provide inconclusive results. Currently, India lacks the precise statistics of BPRD in children due to lack of resources, restricted access to health care center, nephrologist and non-affordability of renal transplant therapy [15]. The present study revealed that nephrotic syndrome (79.91%) was the most common indication followed by lupus nephritis (5.19%) among the children at this center. Histopathological diagnosis identified majorly MCD in 47.63% paediatric population that was comparable to previously reported studies [16,17]. [Table/Fig-3] summarises different renal biopsies conducted in children across India [18-23]. These studies revealed indications, histopathological patterns, and epidemiology of renal diseases in Indian children. Indian studies show that primary glomerular diseases are more common, of which FSGS and MCD are most frequently occurring diseases. FSGS is another major cause of both idiopathic and difficult NS that is observed in the present study with 22.12% [24,25]. Among secondary glomerulonephritis, lupus nephritis was a common indication. Studies documented in literature revealed that primary glomerular diseases are more common than secondary glomerular diseases [26,27]. The present study revealed NS as the most common indication, of which SDNS

Histopathological finding	Number of patients (n=443)
Minimal change disease	211 (47.63)
Focal segmental glomerulosclerosis	98 (22.12)
IgA nephropathy	22 (4.96)
IgM nephropathy	18 (4.06)
Stage IV lupus nephritis	12 (2.71)
Rapidly progressive glomerulonephritis	10 (2.25)
Membranous nephropathy	7 (1.58)
C1Q nephropathy	7 (1.58)
MPGN	6 (1.35)
Chronic interstitial nephritis	6 (1.35)
Stage III lupus nephritis	6 (1.35)
MesPGN	5 (1.12)
DPGN	5 (1.12)
Henoch-Schönlein Purpura (HSP) nephritis	5 (1.12)
Acute interstitial nephritis	4 (0.90)
Stage V lupus nephritis	3 (0.68)
PIGN	3 (0.68)
Thrombotic Microangiopathy (TMA)	3 (0.68)
Diffuse mesangial sclerosis	2 (0.45)
Stage II lupus nephritis	2 (0.45)
Acute or chronic interstitial nephritis	2 (0.45)
Acute tubular necrosis	2 (0.45)
Non-Hodgkin lymphoma	1 (0.22)
Alport syndrome	1 (0.22)
Antibody mediated rejection (ABMR)	1 (0.22)
TBMN	1 (0.22)

[Table/Fig-2]: Histopathological findings in patient.

Data shown as n (%), unless otherwise specified; DPGN: Diffuse proliferative glomerulonephritis;

MesPGN: Mesangial proliferative glomerulonephritis; MPGN: Membranoproliferative glomerulonephritis;

PIGN: Post infectious glomerulonephritis; TBMN: Thin basement membrane nephropathy

accounted for highest number of cases that was in accordance with the study reported by Kanodia KV et al., [21].

A similar retrospective study was reported by Lee S et al., comprising 318 children with a mean age of 9.7 years and male predominance (64.5%). It was reported that 35.9% with asymptomatic urinary abnormalities and 21.30% MCD cases after histopathological diagnosis followed by renal biopsy [13]. Another study by Özkayın N et al., presented a 10-year data of renal biopsies performed on children in Turkey having majority of girls (54%) with NS as the main indication that is contradictory to other reported studies wherein percentage of boys was higher [28]. Medical literature shows the presence of major diagnosis in children with NS constituting almost 40% of cases [29,30]. A cohort study of renal biopsy indicated NS as the commonest indication in the children with median age of 10.4 years followed by proteinuria [26].

The biopsy findings in children with NS revealed SDNS as the most common indication. These findings are in accordance with the reported literature by Printza N et al., wherein a retrospective study in children done for over 7 years showed SDNS as the most common indication along with FSGS as most frequent occurring BPRD [31]. MCD (47.63%) and FSGS (22.12%) were the common histopathological findings followed by IgA Nephropathy (4.96%) and IgM Nephropathy (4.06%). Similar findings were reported by Mohapatra A et al., in a study conducted in South Asian children and another Indian study by Nammalwar BR et al., having MCD

Parameters	Sarwal D et al., 2019 [18]	Muthu V et al., 2018 [19]	Sinha R et al., 2016 [23]	Gunasekaran K et al., 2015 [20]	Kanodia KV et al., 2015 [21]	Chandrika BK 2009 [22]
Study period	2007-2016	2009-2012	2012-2014	2013-2014	2008-2013	-
Sample size	83	177	100	83	335	1592
Age (years)	2-18	13-19	0.3-17	1-13	≤14	5-78
Region	North India	Northwestern India	Kolkata	South India	Ahmedabad	Kerala
Primary GN	89.2	84.8		-	81.8	-
FSGS	22.9	30.0	25	-	8.0	11.9
MCD	36.1	25.3		-	6.93	-
MN	7.2	-		-	6.3	-
PIGN		-		86.7	9.6	-
Crescentile GN	4.8	-		-	10.9	12.3
MPGN	6.0	-	6	1.2	13.5	1.3
IgAN	2.4	11.4	6	1.2	6.2	14.26
IgMN			10		14.9	
DPGN	4.8	6		-		
MesPGN	3.6	-		2.4	24.5	27.3
Secondary GN	7.2	15.25		-	16.1	-
LN	6.0	70.4		2.4	7.8	-
Amyloidosis	1.2	7.4		-	0.89	-
TIN	3.6	-		-	-	-
AIN/ATN	3.6	-		-	-	-
HUS					6.3	
HTN					1.2	
Miscellaneous	-	2.7	11	2.4	-	-

[Table/Fig-3]: Renal biopsy studies conducted in children across India in past 10 years [18-23].

Data is presented as % unless otherwise specified. AIN: acute interstitial nephritis; ATN: Acute tubular necrosis; DPGN: Diffuse proliferative glomerulonephritis; FSGS: Focal segmental glomerulosclerosis; GN: Glomerulonephritis; IgAN: IgA nephropathy; IgMN: Ig membranous nephropathy; LN: Lupus nephritis; MCD: Minimal change disease; MN: Membranous nephropathy; MPGN: Membranoproliferative glomerulonephritis; MesPGN: Mesangial proliferative glomerulonephritis; PIGN: Post infectious glomerulonephritis; TIN: tubulointerstitial nephritis; HTN: Hypertensive nephropathy; HUS: Hemolytic uraemic syndrome

the most frequent diagnosis with NS [32,33]. India and many other countries show prevalence of primary glomerular diseases than secondary with NS as the major biopsy proven indication and MCD followed by FSGS are major histological findings.

LIMITATION

This was a single center study; however, the results can boost to conduct similar studies and surveys at other regions to determine the current trend in paediatric renal biopsies. Electron Microscopy (EM) data was not included as it is not performed in the center due to lack of resources.

CONCLUSION

Nephrotic syndrome was the most common indication in children with SDNS in the present retrospective study. MCD was the most common histopathological finding followed by FSGS and IgA nephropathy. This study revealed an 8-year overview of renal diseases in paediatric population of Eastern India highlighting the importance of renal biopsy as a diagnostic tool in guiding to tailor the treatment strategy.

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