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Spectrum of Renal Diseases in a Tertiary Care Hospital in North-west India: A Biopsy-based Retrospective Study in Pediatric and Adult Population.

[1]Manoj Kumar, Assistant Professor, Department of Pediatrics, J L N Medical College, Ajmer.
[2]Swati Swati , Assistant Professor, Department of Obstetrics & Gynecology, NMCH, Rohtas.
[3]Anjali Kumari, Resident, Department of Obstetrics & Gynecology, DMCH, Darbhanga
[4]Hemrajani Deepika, Professor, Department of Pathology, SMS Medical College, Jaipur
Corresponding Author: Manoj Kumar, Department of Pediatrics, JLN Medical College, Ajmer, India

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Abstract

Background: Most cases of renal diseases respond to conservative management, but renal biopsy is required in significant number of cases. The knowledge of biopsy-proven incidence of renal pathologies according to age, sex, race, geographic location and clinical presentation is helpful to the clinicians in understanding the spectrum of renal diseases in their clinical settings.

Material and Methods: A retrospective study was done to analyse the biopsy of renal disease in SMS Medical College, Jaipur over duration of 39 months (February 2013 to April 2016). All renal biopsies were analysed by light and immune-fluorescence microscopy and were classified as primary glomerular disease (PGD), secondary glomerular disease (SGD) and tubulo-interstitial nephritis (TIN).

Results: 254 cases were included in this study. 149 belonged to adult group and 105 to pediatric group. Age range in pediatric group was 45 days to 20 years (mean 11.85 years). 59.05% were male, whereas female were 40.95%. Adult's age range was 21 to 80 years (mean 51.9 years) with 64.43% male and 35.57% female. Nephrotic syndrome was the commonest indication for renal biopsy in both age groups. Minimal Change Disease (MCD) was the most common reporting in children and adults, followed by Focal Segmental Glomerulosclerosis (FSGS) and lupus nephritis (LN) in pediatric group & tubulo-interstitial nephritis (TIN) and FSGS in adults.

Conclusion: MCD continues to be the commonest pathology in all age groups followed by FSGS and Lupus nephritis in pediatric population, whereas TIN is the second most common finding in adults followed by FSGS.

Keywords: FSGS, Lupus nephritis, MCD, renal biopsy, TIN.

Introduction

With the increasing trends in use of renal biopsy as a confirmatory modality in renal pathology, it is becoming easier for the clinicians to provide appropriate planning and management and further prediction of recurrences of renal diseases. Since the incidence and prevalence of renal

diseases are affected by various factors such as age, sex, race, economic status, local prevalent infection, environmental condition, genetic makeup of patients , clinical condition, it is important to observe the role of these factors and study the trends in the occurrence of renal diseases. In India there is a lack of national registry database for biopsy proven- renal diseases. The studies of renal biopsies done for various indications in different geographic locations will be very helpful to determine and understand the changing patterns in renal diseases. This study is done in a tertiary care hospital in the north western part of India based on biopsy of renal diseases done for the various indications in paediatric and adult age group.

Kidney diseases impose a considerable degree of financial burden on the patients as well as the government hospitals. Understanding of the underlying histo-pathology responsible for the clinical manifestations in different clinical settings can be of great help in appropriate clinical management of the various renal diseases. Studies have shown that Mininmal Change Disease (MCD) remains the most frequent underlying histo-pathology for nephritic syndrome in the areas of Maharashtra (Mumbai)[1] and Vishakhapatnam (South-India)[2] . On the other hand, one study in South India[3] in Mysore had shown Membranoproliferative Glomerulonephritis (MPGN) as the leading histology found in cases of nephrotic syndrome. So understanding of these patterns is helpful to physicians, paediatricians and nephrologists all over the country in managing the treatment response. Not only lies the importance of this study at national level, but at international level too histological findings are helping in patient care led by the different hospitals in different countries due to immigration and emigration. As for example in the era of 1995-1997 IgA nephropathy was the most common glomerulonephritis found in Australia[4]. So we have undertaken this study in a centre of North-west India to reflect the recent trends in this geographical location.

Material and Methods

This study is a retrospective study done in the Department of Pathology, at SMS Medical College, Jaipur. With the due permission from the required authorities, clinical data of all the patients in paediatric and adult age groups undergoing renal biopsies in the hospitals attached to the college was retrieved. All the relevant information of patients like name, age, sex, clinical status with respect to renal disease, laboratory findings like CBC, serum creatinine, blood urea, ABG, urinary protein (24 hours and dipstick), serological data like antinuclear antibodies , anti-neutrophil cytoplasmic antibodies, anti double stranded DNA, C3 complement level, and ultrasound of abdomen (KUB) if available were collected along with the indications for renal biopsy. Exclusion criteria were: 1. Inadequate sample; 2. Second, or repeat biopsy; 3. Allograft renal biopsies (renal transplant cases); and 4. Normal histology reporting.

The total number of renal biopsies performed from February 2013 to April 2016, over a period of 39 months in the SMS Medical college, Jaipur was 285. After excluding 31 cases, the total number of cases included in the study were 254.The indications for renal biopsies were divided into groups like nephrotic syndrome (proteinuria $\geq$ 3.5 g/day $\pm$ hypoalbuminemia), nephritic syndrome (hematuria, RBC casts and a <3-month history of proteinuria <3.5g/day), systemic lupus erythematosus (SLE), chronic kidney disease(CKD = proteinuria 1-3.5 g/day $\pm$ GFR <60ml/min/1.73m^2 for >3-month history), haemolytic uremic syndrome (HUS), rapid progressive renal failure (RPRF = acute deterioration of renal

function, such as a 2-fold increase in serum creatinine or a 50% decrease in creatinine clearance), and unexplained renal failure (URF) . These clinical conditions were defined as per standard definitions/terminologies. The biopsy samples were sent (one in normal saline and other in formalin) and processed as per the standard protocols and were subjected to light microscopy and immune-fluorescence microscopy techniques. Different types of stains like Hematoxylin and Eosin, Periodic acid Schiff, Masson's trichrome, Silver methanamine, Congo red were used as per requirements. Cases included in the study were broadly classified and studied into two groups: pediatric age group (≤20 years) and adult age group (≥21years to 80 years). The biopsy findings were divided as: primary glomerular diseases (PDG), secondary glomerular diseases (SGD) and tubulo-interstitial nephritis (TIN). Minimal change disease (MCD), Focal-segmental glomerulosclerosis (FSGS), membranous glomerulopathy, membranoproliferative glomerulonephritis (MPGN), diffuse-proliferative glomerulonephritis (DPGN), chronic glomerulonephritis, crescentric glomerulonephritis, IgA Nephropathy, C3 glomerulopathy, post infectious glomerulonephritis (PIGN), Alport's syndrome, infantile nephrotic syndrome and congenital nephrotic syndrome were kept under primary glomerular disease (PGD). Secondary glomerular diseases (SGD) included: lupus nephritis, diabetic nephropathy, amyloidosis, and calcineurin inhibitor (CNI) toxicity). Relevant statistical analysis was carried out as required.

Results

In the pediatric age group, 45 days was the lowest age for which renal biopsy was performed and its indication was congenital nephrotic syndrome. The upper age limit in pediatric group was 20 years. The mean age was calculated as 11.8 yrs. The age range for adult group was 21 years to 80 years and the calculated mean age at presentation in adult cases was 51.9 years.

The pediatric group (n = 105) had 59.05% male and 40.95% female cases [62 male, 43 female]. In adult group (n = 149), 64.43% were male (n = 96) and 35.57% female (n = 53).

In the male group of pediatric patients (n = 62), maximum cases belonged to age group 6-10 years (n = 18, 29.03%), followed by 16-20 years (n = 17, 27.41%). Amongst female pediatric cases (n = 43), maximum belonged to 16-20 years age group (n = 15, 34.88%) followed by 11-15 years age group (n = 14, 32.56%) **{Table no. 1}**. Maximum cases of male adults undergoing renal biopsy belonged to age groups 21-30 years (n = 47, 48.96%), followed by 31-40 years (n = 28, 29.17%). Maximum number of female adults belonging to age range 31-40 years (n = 21, 39.62%) underwent renal biopsy which was followed by age group 21-30 years (n = 16, 30.19%) **{Table no. 2}**.

Nephrotic syndrome was the most common indication for renal biopsy in 55.24% pediatric (n = 58) and 28.18% adult (n = 42) patients. This was followed by nephritic syndrome (29.52% in pediatric age, 24.16% in adult age). Both these indications had a male preponderance. SLE as an indication for renal biopsy was more common in females than in males in both pediatric (3 male, 7female, ratio M:F = 1:2.33) and adult (2 male, 14 female, ratio M:F = 1:7) groups. More numbers of adult males were sent for biopsies in cases of CKD but in pediatric group only 3 females had biopsy for this indication, and no males **{Figure no.1 & 3}**.

In pediatric cases (n = 105), PGD (n = 91, 86.67%) was in much excess [~ 7.58 times] as compared to SGD (n = 12, 11.43%) **{Table no.1}**. In adults (n = 149) also

PGD (n = 100, 67.11%) outnumbered the cases of SGD (n = 30, 20.13%) by more than 3 times **{Table no.2}**. TIN was found more commonly in adults when compared to pediatric group. This shows SGD and TIN increase with age.

In the pediatric age group (n = 105), most common histo-pathology being found was MCD (n = 38, 36.19%), followed by FSGS (n = 11, 10.47%) and lupus nephritis (n = 10, 9.52%). MPGN, DPGN and C3 glomerulopathy were found to be equally prevalent in pediatric age group i.e. 6.67% each (n = 7 each) **{Figure number 2}**.

MCD (n = 23, 15.43%) is the most common histology in adult age group (n = 149). This is followed by TIN (n = 19, 12.75%) and then FSGS (n = 18, 12.08%). Chronic glomerulopathy (n = 15, 10.08%), lupus nephritis (n = 14, 9.4%), MPGN (n = 13, 8.72%), and membranous nephropathy (n =13, 8.72%) have similar degree of prevalence in adults, i.e. 8-10%. Amyloidosis (n=7, 4.69%), C3 glomerulopathy and CNI toxicity (n = 5, 3.36% each) and diabetic nephropathy (n = 4, 2.68%) accounted for lesser number of biopsy-proven renal pathologies **{Figure number 4}**.

Fig.1 Gender-wise clinical indications for renal biopsy in pediatric patients {n = 105}

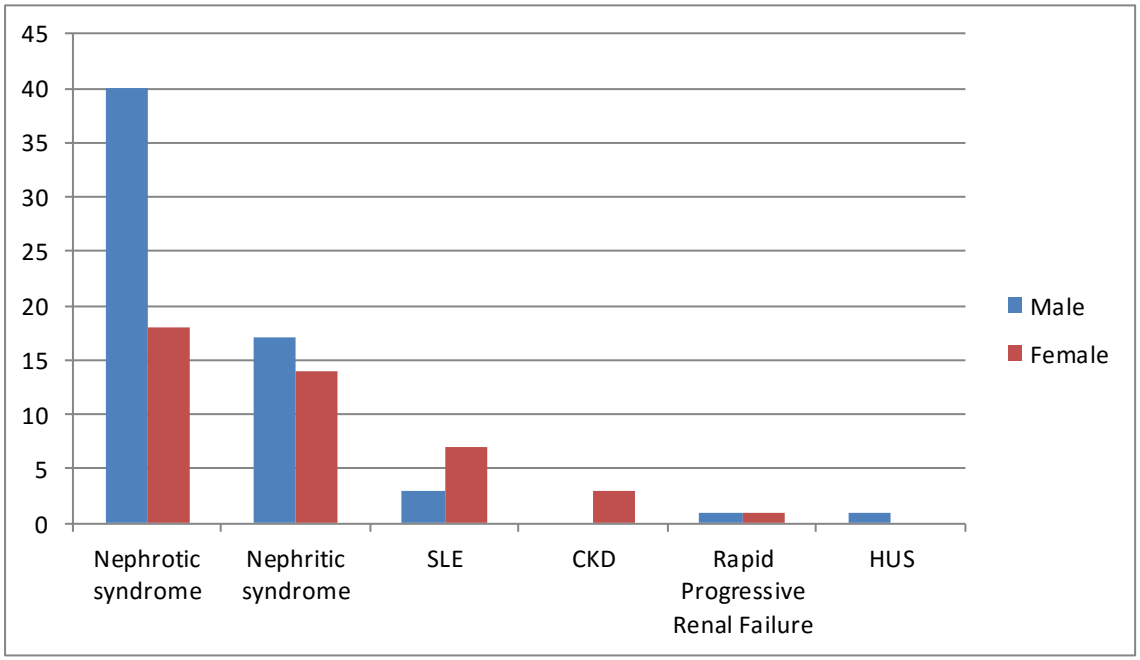


Table 1: Age & gender based distribution of renal histopathology in pediatric patients

S. no.	Age → Histo-pathology ↓	0-5 years		6-10 years		11-15 years		16-20 years		Total (%)
		M	F	M	F	M	F	M	F	
Primary Glomerular Diseases { PGD = 86.67%, n = 105 }										
1.	MCD	9	5	7	4	5	1	6	1	38 (36.19%)
2.	FSGS	1	1	3	0	1	2	1	2	11 (10.47%)
3.	MPGN	0	0	1	1	3	0	1	1	7 (6.67%)
4.	IgA nephropathy	1	0	0	0	0	1	1	1	4
5.	Membranous GN	0	0	0	0	1	0	1	0	2
6.	Crescentric GN	0	0	1	0	1	0	0	0	2
7.	DPGN	0	0	2	1	0	3	1	0	7
8.	Chronic GN	0	0	0	0	0	1	1	3	5
9.	Alports's ds	0	0	0	0	0	0	1	0	1
10	C3 glomerulopathy	0	0	2	0	1	1	2	1	7
11	PIGN	0	0	1	0	1	2	0	1	5
12	Infantile nephrotic s.	1	0	0	0	0	0	0	0	1
13	Congenital nephrotic s.	0	1	0	0	0	0	0	0	1
Total (PGD)		12	07	17	06	13	11	15	10	91
Secondary Glomerular Diseases {SGD = 11.43%}										
1.	Lupus nephritis	0	1	1	0	1	2	0	5	10 (9.52%)
2.	Diabetic nephropathy	0	0	0	0	0	1	0	0	01
3.	Amyloidosis	0	0	0	0	0	0	1	0	01
Total (SGD)		00	01	01	00	01	03	01	05	12
TIN {1.9%}		1	0	0	0	0	0	1	0	02
Total		13	08	18	06	14	14	17	15	105
n = 105										

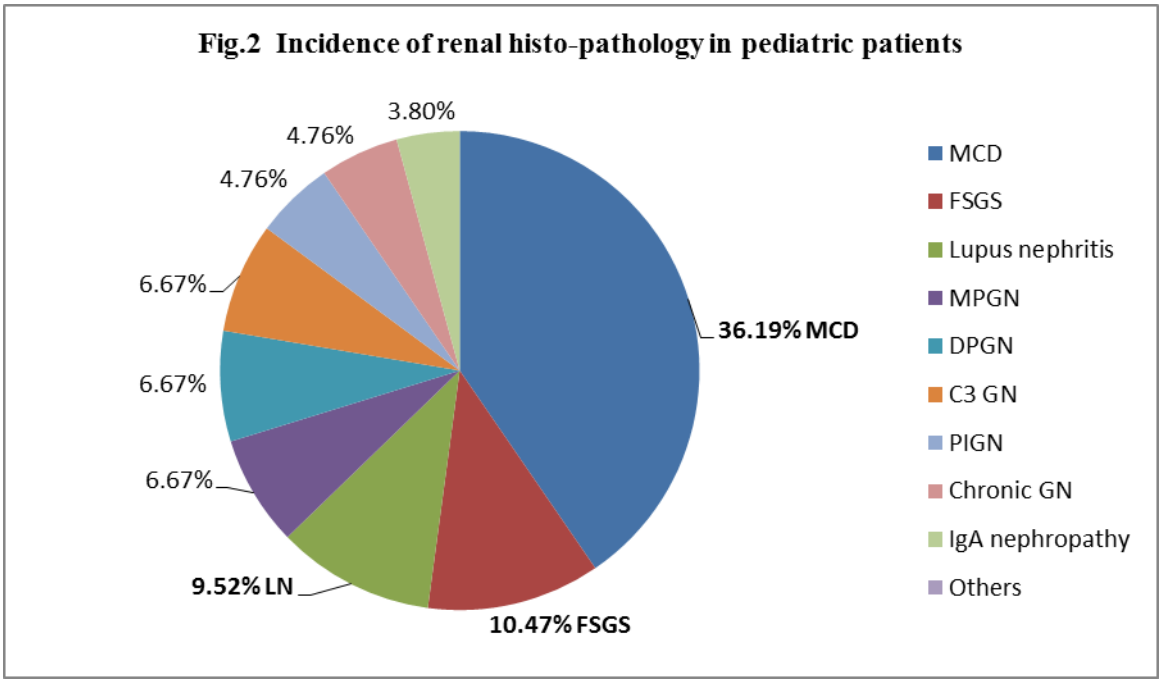


Figure 3: Gender-wise clinical indications for renal biopsy in adult patients {n = 149}

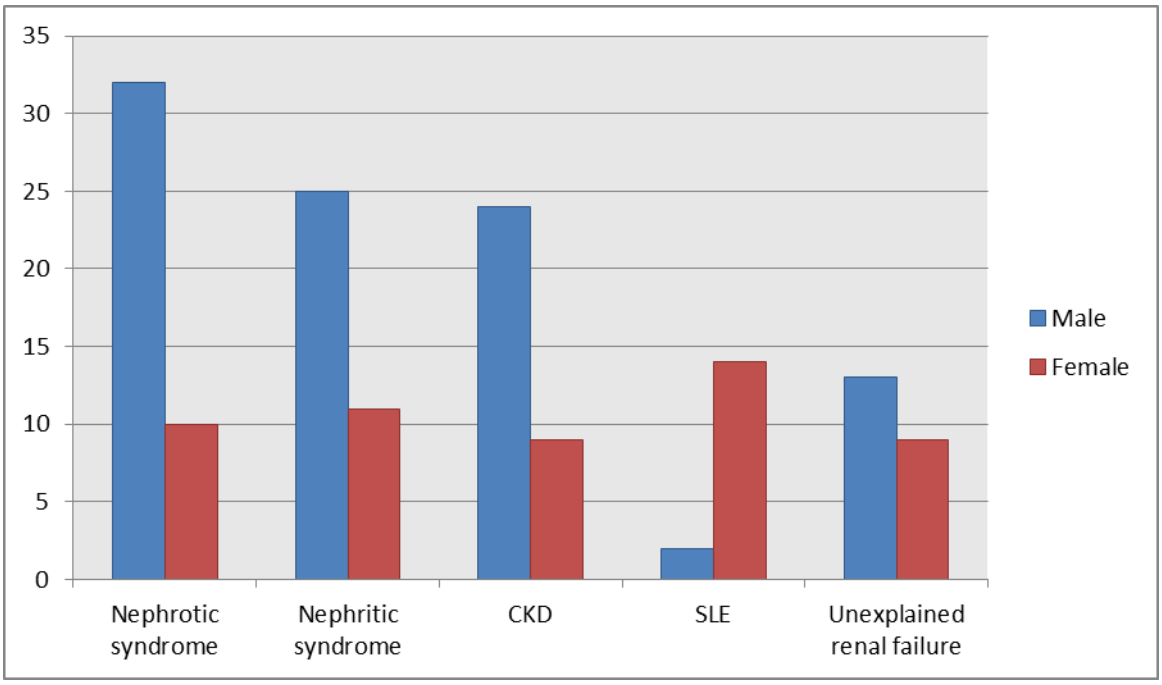
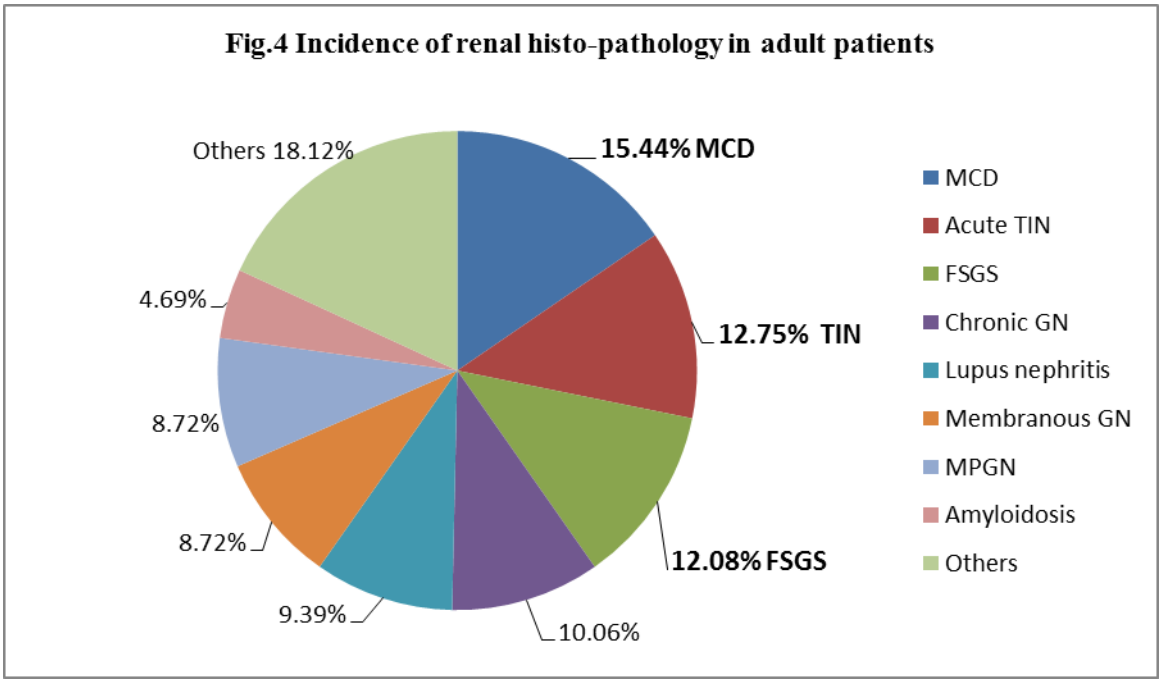


Table no. 2: Age & Sex wise distribution in adult cases of renal biopsies

Sn.	Age → Histo-pathology ↓	21-30 years		31-40 years		41-50 years		51-60 years		61-70 years		71-80 years		Total (%)
		M	F	M	F	M	F	M	F	M	F	M	F	
PRIMARY Glomerular Diseases {PGD} [67.11%, n=149]														
1.	MCD	9	2	4	2	0	1	1	1	1	1	1	0	23 (15.44%)
2.	FSGS	8	2	1	4	0	1	0	1	1	0	0	0	18 (12.08%)
3.	MPGN	6	0	2	2	1	1	0	1	0	0	0	0	13 (8.72%)
4.	IgA nephropathy	2	1	1	0	0	0	0	0	1	0	0	0	05
5.	Membranous GN	2	1	3	1	3	0	0	1	1	1	0	0	13 (8.72%)
6.	Crescentric GN	1	0	0	0	0	0	0	0	0	0	0	0	01
7.	DPGN	1	1	1	1	0	0	0	0	0	0	0	0	04
8.	Chronic GN	7	3	2	1	2	0	0	0	0	0	0	0	15 (10.07%)
9.	Alports's ds	0	0	0	0	0	0	0	0	0	0	0	0	00
10	C3 glomerulopathy	0	2	1	0	2	0	0	0	0	0	0	0	05
11	PIGN	1	0	2	0	0	0	0	0	0	0	0	0	03
Total		37	12	17	11	8	3	1	4	4	2	1	0	100
SECONDARY Glomerular Diseases {SGD 20.13%}														
1.	Lupus nephritis	1	4	0	8	0	1	0	0	0	0	0	0	14 (9.39%)
2.	Diabetic nephropathy	1	0	2	0	0	0	0	0	0	1	0	0	04
3.	CNI toxicity	1	0	2	0	0	1	0	1	0	0	0	0	05
4.	Amyloidosis	2	0	1	0	2	0	1	0	1	0	0	0	07
Total (SGD)		05	4	05	08	2	2	1	1	1	1	0	0	30
TIN {12.75%}		5	0	6	2	1	3	0	0	2	0	0	0	19 (12.75%)
Total		47	16	28	21	11	08	02	05	07	03	01	00	149
n=149														



Discussions

Glomerular diseases are influenced by genetic, immunologic, infectious, perfusion, or coagulation factors. There are several mechanisms which cause renal injuries, but the numbers of histo-pathologic responses are limited. Conversely, different disease states can produce similar microscopic changes[5]. So this retrospective study was done over a period of 3 years and 3 months in a tertiary care hospital in North-west India to study the epidemiology and clinical correlation of various renal pathologies. The total numbers of biopsies being studied were 254, 105 in pediatric group (41.34%) and 149 in adult group (58.66%). Low prevalence of renal biopsies in pediatric age group indirectly suggests either hesitancy, or fear of doing renal biopsies, or strict criteria set for renal biopsy, or can be due to higher age at onset of renal diseases. In pediatric age group (n = 105) maximum renal biopsies were performed in the age group 10 to 20 years (n = 60), which accounted for 23.62% cases of total numbers of biopsies that we studied (n = 254). In adult age group, patients in age group 21-40 years (n = 112) underwent the highest number of renal biopsies accounting for 44.09% of total 254 cases. Renal diseases predominated in male (M:F=1.64:1). This is similar to study done by Ramakant Desale et al[1] and many studies in different parts of world also show a male predominance. In pediatric patients, incidence of biopsy-proven renal disease were in order of MCD (31.5%), FSGS (11.7%), Lupus Nephritis (8.1%), DPGN (7.2%). Similar findings were observed in South Indian study with MCD (most common), followed by DPGN, FSGS, Lupus nephritis[6]. In our study MCD was the most common to both male and female patients but 2nd most common condition in male was FSGS whereas in female 2nd most common was Lupus Nephritis suggesting lupus nephritis having female predilection. Nephrotic syndrome was overall the most common indication for renal biopsy in pediatric age group. Similar results with Nephrotic syndrome as the most common indication for biopsy were reported from other parts of world i.e. South India[7], Morocco[8], Serbia[9], Pakistan[10], Saudi Arabia[11]. But many studies from

different parts of the world reported IgA Nephropathy as the commonest type of glomerulonephritis: 50% in China [12, 13], 34% in Australia[4], 28% in Korea[14] and 21% in USA[15]. Most European studies have also shown IgA Nephropathy to be the most common type of glomerulonephritis, though with variable percentages: 37% in Italy[16] and 34% in the Czech Republic[17]. Its incidence in Spain was 17%[18] and 15% in Lithuania[19]. On the contrary, IgA nephropathy was seen in only 3.8% of pediatric cases and 3.35% of adult cases in our study. Though IgA nephropathy is the most common glomerular disease worldwide, few studies from Pakistan[10] and West Asian countries (Bahrain[11] and Iran[20]) showed IgA nephropathy as the least frequent primary glomerulonephritis. This variation may be due to underestimated incidence, or may be due to reluctance in conducting biopsy, or lack of mass screening program or biopsy facility in the concerned areas or may be due to genetic make-up differences. Worldwide the most common histological finding in nephritic syndrome is membranous nephropathy, few studies from Europe and Australia suggest FSGS as the leading cause for nephritic syndrome[15]. In India membranous glomerulonephritis is the most common pattern in South India study, MCD in North India study[1]. In our study the commonest cause was MCD followed by MPGN, FSGS and MGN, which are similar to other studies conducted in India [21]. The overall incidence of secondary glomerular disease (SGD) in our study was 16.54%.In pediatric age group (n = 149) its incidence was 11.43% (n = 12) and in adult this data was 20.13% (n = 30). Pediatric SGD (n = 12) is accounted by maximum number of lupus nephritis (n = 10, 83.33%) followed by amyloidosis and diabetic nephropathy (n = 1 each, 8.33% each). The most common SGD in adult age group (n = 30) was again lupus nephritis (n = 14, 46.67%), amyloidosis (n = 7, 23.33%), CNI toxicity (n = 5, 16.67%) and diabetic nephropathy (n = 4, 13.33%). TIN was less common in pediatric population (1.9%), but it was found in 12.75% of adults undergoing biopsy. This shows TIN increases with age, as does the SGD.

Conclusion

In North-west India, MCD still continues to remain the leading histological finding in both adult- and pediatric-age groups. However, it is much more common in pediatric cases, and as age advances its incidence decreases. FSGS, MPGN, LN and TIN become more common with increasing age. LN is the most common SGD in both age groups.

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