Original Article

HISTOLOGY PERSPECTIVE OF CHILDHOOD RENAL DISEASES- A SINGLE CENTRE EXPERIENCE

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ABSTRACT:

BACKGROUND:

There is not much information regarding the prevalence of different renal diseases in paediatric population in Pakistan due to lack of central data. A few studies have been previouslypublished from individual centres. This study reflects the different histology patternsof renal diseases in children in our centre.

OBJECTIVES:

To assess the indications for kidney biopsy and determine the different histology patterns of renal diseases in paediatric patients in our centre.

SUBJECTS AND METHODS:

This retrospective study has been conducted at The Children's Hospital and The Institute of Child Health Lahore from February 2014 to February 2015. The data has been collected from the renal biopsy record of Paediatric Nephrology department. The paediatric patients of either sex aged less than 16 years diagnosed with renal diseases that required renal biopsy were included in the study.

RESULTS:

Out of the total of 159 patients, 102(64.2%) were males and 57(35.8%) were females. The age range was 0.7 years to 16 years, mean age= 7.86 years and SD $\pm$ 4.00. The most common indications for renal biopsy were steroid resistant nephrotic syndrome (SRNS), atypical nephrotic syndrome and lupus (SLE) nephritis.The most common histology reportedwas Mesangioproliferative Glomerulonephritis in 71(44.7%) patients followed by Membranoproliferative Glomerulonephritis in 36(22.6%)whilelupus nephritis was seen in(18)11.4% patients.

CONCLUSIONS:

The most common indication of renal biopsy was SRNS and the frequent histology reported was Mesangioproliferative Glomerulonephritis. SLE nephritis also prevails in large number of paediatric patients.

KEY WORDS: Renal biopsy, Renal diseases, Histology, Children.

INTRODUCTION:

Percutaneous renal biopsy is the main procedure in paediatric nephrology for establishing diagnosis and therapy guidance in kidney diseases[1]. Initially the renal biopsy

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used to be an open surgical procedure as reported by Gwyn NB[2]. Though the first percutaneous renal biopsy was described in 1934,[3] the procedure was performed in 1951 by Iversen and Brun[4]. With progress in technology and imaging, renal biopsy became a safe procedure[5]. In paediatric patients percutaneous renal biopsy was firstreported by Galan and Maso[6] in 1957 in the study ofnephrotic patients.Renal biopsy in children is more challenging and difficult than the adult patients as it not only requires expertise but also skillful handling of anxious young patients along with counseling of parents regarding the safety and efficacy of this invasive procedure[7].Renal biopsy data from different centres gives an estimated view into the epidemiology of renal diseases in children, as well as forms an important basis for paediatric nephrologists to improve treatment[8,9].The prevalence of biopsy-proven renal diseasepattern varies according to race, age, geographic distribution, socioeconomic conditions and different indications for renal biopsy[10]. Though renal biopsy as procedure and prevalence of different histopathological patterns of kidney diseases in children have been reported, yet the data of renal disease mostly in adults is available from large national renal biopsyregistries from Europe and other countries, while paediatric data is scarce[11].

The objective of this study is to assess the indications for kidney biopsy in paediatric patients and determine the common histology patterns of renal diseases among Pakistani children based on the results of renal biopsies.

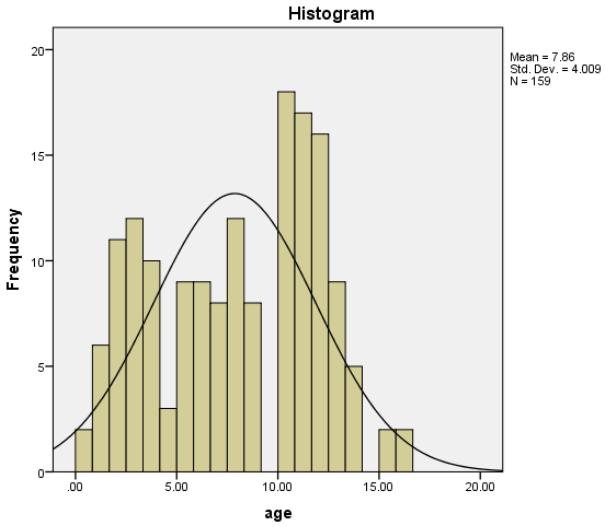
SUBJECTS AND METHODS:

This study has been conducted in the Department of Paediatric Nephrology at The Children's Hospital and The Institute of Child Health Lahore over a period of one year from 15 February 2014 to 14 February 2015. The data has been collected retrospectively from the renal biopsy record maintained by the department. The paediatric patients of either sex aged less than 16 years, diagnosed with renal diseases that required renal biopsy, were included in the study. Data was collected and retrieved from medical records and entered on a specified form regarding age, sex, indications for renal biopsy and histopathological diagnoses. Renal biopsy was performed after the written consent was taken from the parents. The pre-requisite laboratory investigations for renal biopsy included complete blood count (hemoglobin, hematocrit, white cell count and platelet count), coagulation profile (prothrombin time, activated partial thromboplastin time) and renal function tests. Children excluded from the study were those with bleeding diathesis, marked azotemia, scarred kidneys (detected by ultrasound at the time of renal biopsy) and those for whom consent for the procedure was refused. In hypertensive patients renal biopsy was performed after the blood pressure was controlled.The procedurerequired sedation with chloral hydrate and midazolam/pentazocin while nalbuphine was given for pain relief. The renal tissue was obtained fromthe lower pole of either kidney with automated biopsy gun under ultrasound guidance. Two samples of renalbiopsy were routinely obtained for complete pathological evaluation and biopsy tissue was fixed in 10% buffered formalin.One renal biopsy core was sent to histopathology department and processed in automatic tissue processor for light microscopy (LM) and immunostains while the other biopsy core was sent for immunoflourescence (IF) study. All biopsies were analyzed using the SPSS version 20.0.

RESULTS:

There were a total of 159 patients enrolled in the study of whom 102(64.2%) were males and 57(35.8%) females. The age range was from 0.7 years to 16 years with mean age = 7.86 years and SD $\pm$4.00. The age distribution is shown in Figure I. The most common indication for renal biopsy was steroid resistant nephrotic syndrome (SRNS) followed by atypical nephrotic syndrome and SLE nephritis. The most common disease reported on histology was Mesangioproliferative Glomerulonephritis as was seen in 71(44.7%) patients. The second most common histological presentation was Membranoproliferative Glomerulonephritis 36(22.6%) while SLE nephritis accounted for 18(11.4%) patients.The World Health

Organization (WHO) classification was used for staging of SLE nephritis -SLE nephritisII was present in 9(5.7%)patients while SLE nephritis III and IV were seen in 2(1.3%) and 7(4.4%) respectively. The pathology of Focal Segmental Glomerulosclerosis was found in 9(5.7%) while Minimal Change disease (MCD) was down the list of steroid resistant nephrotic syndrome as only 5(3.1%) patients showed normal histology.



There were 6(3.8%) patients with Rapidly Progressive Glomerulonephritis (RPGN) and the remaining histopathological diagnoses are shown in TableI. Inconclusive renal biopsy was reported only in 3(1.9%) patients as a consequence of obtaining inadequate tissue. Table II shows the gender based disease prevalence. Mesangioproliferative glomerulonephritis accounted for 48 males and 23 females, while Membranoproliferative glomerulonephritis was seen in 36 patients - 24 males and 12 females. The data of patients with SLE nephritis revealed more prevalence among males in SLE nephritisII as compared to SLE nephritisIII/IV which was more common in females. RPGN was seen to be common among male patients.

DISCUSSION:

Renal biopsy indications include steroid resistant nephrotic syndrome(SRNS), atypical presentation of nephrotic syndrome i.e. age less than one year or more than 10 years, gross hematuria, low serum C3, persistent diastolic hypertension, renal impairment, steroid-dependent and / or frequent relapsing nephrotic syndrome, before initiation of immunosuppressive therapy (particularly cyclosporine), systemic diseases with renal manifestations, chronic kidney disease of unknown etiology, acute kidney injury with unexplained cause, RPGN and hematuria with no pathological diagnosis.Another indication can be to monitor the prognosis of disease and response to treatment. SRNSpatients included in our studywere those whofulfilled the definition criteria– children who did not achieve remission after induction therapy with steroids (prednisolone) for four weeks[12]. SLE patients were included who fulfilled the criteria of the American College of Rheumatology[13]. In paediatric patients there is increased risk for renal involvement as compared to adults with SLE and about 10% to 30% patients progress to end stage renal disease[14]**.**

Various observational studies have been conducted worldwide in paediatric patients to elucidate the histological patterns of renal diseases.The frequency of different histological patterns ofrenal disease has been linked to multiple factors like age, sex and response to treatment[8].Some studieshave also been reported from Pakistan taking paediatric populationunder consideration and finding the most common histological pattern of renal disease among them. A study by Hafeez F et al[15] showed Mesangioproliferative glomerulonephritis as the most common glomerulopathy in paediatric patients presenting with atypical nephrotic syndrome which is similar to the findings of our study. Another study conducted by Mubarak M et al[16] in both adult and paediatric population showed Minimal change disease (43.8%) as the leading histology followed by Focal segmental glomerulosclerosis (38.14%). Another study by Lanewala A et al[17] was done by compiling the data of 13 years showing the glomerulopathies to be the commonest histological diagnosis comprising 93.34% of all biopsies - Primary glomerular disease accounted for 87.64%withMinimal change disease found in 29.4% patients and Focal segmental glomerulosclerosis in 21.8% of

cases. Although secondary glomerulopathies accounted for 5.7% cases, lupus nephritis was the commonest similar finding in lieu of our study which showed primary glomerulopathies the leading diagnosis followed by lupus nephritis 76.1% and 11.4% respectively.
In another retrospective study by Moorani KN et al[18] done at one of the tertiary care centres showed the male to female ratio of kidney diseases in paediatric population to be 1.1:1 while in our study the ratio is almost 1.8:1 as over last few years the incidence of kidney diseases in is increasing in male population. In their study the leading indication for renal biopsy was primary glomerulopathies seen in 84.74% patients while SLE nephritis accounted for 9.325 cases as compared to our study. One retrospective study done by Ali A et al[19] in northern Pakistan showed the male to female ratio of 1.6: 1, almost equivalent to our study. The main indication of renal biopsy in their study was idiopathic nephrotic syndrome as it constituted about 74% of biopsy specimens including SRNS- Focal segmental glomerulosclerosis and Mesangioproliferative glomerulonephritis being the common histological diagnoses in 18.30% and 17.83% cases respectively. Their study showed RPGN in about 4.34% in contrast to our study in which it was seenin 3.8% cases whileSLE nephritis was described in only 0.96% patients as compared to our study which showed 11.4% such patients.

A retrospective study published by Rabbani MA et al[20] in Aga Khan University hospital Pakistan collected data for about two decades in adult patients. Theyreported the histology of primary glomerulopathies in 49% patients and SLE nephritis in 34% cases. Another retrospective study by Mubarak M et al[21]in adult patients showed the primary glomerulonephritis in 86.9% and SLE nephritis in 44.1% patients followed by amyloidosis and diabetic nephropathy in 42.1% and 8.1% respectively.In one of the publications by Bakr A et al,[22] Egyptian children showed the primary glomerular disease as the most common histology (67.4%) followed by secondary glomerulonephritis in 19.4%with SLE nephritis constituting about 17% of these cases. The limitation to our study is its retrospective design. As this is not a national survey, rather it is a single-center study, indications of renal biopsy may have affected the percentage of frequency of different renal diseases.

CONCLUSION:

Though this study is not the first pediatric report of renal histopathological findings, it has been reported from one of the main tertiary care hospitals in Pakistan. SRNS was found to be the most frequent indication of renal biopsy in our patients with Mesangioproliferative glomerulonephritis being the commonest histological diagnosis. SLE nephritis is also one of the major diseases in paediatric patients. This study enables the comparison of indications for renal biopsy in paediatric patients and gives spectrum of prevalence of different renal diseases based on histological pattern as compared to different studies published previously.

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Table I: Frequency of different diseases on histology basis

Histopathological Diagnosis	Frequency	Percent
Chronic Pyelonephritis	1	0.6
End Stage Renal Disease	4	2.5
Focal Segmental Glomerulosclerosis	9	5.7
HSP Nephritis	2	1.3
IgA Nephropathy	1	0.6
Inconclusive	3	1.9
Interstitial Nephritis	2	1.3
Minimal Change Disease	5	3.1
Mesangioproliferative Glomerulonephritis	71	44.7
Membranoproliferative Glomerulonephritis	36	22.6
Polycystic Kidney	1	0.6
Rapidly Progressive glomerulonephritis	6	3.8
SLE Nephritis-II	9	5.7
SLE Nephritis-III	2	1.3
SLE Nephritis-IV	7	4.4
Total	159	100.0

Table II: Gender and histology based disease frequency

Histopathological Diagnosis	Gender		Total
	Male	Female	
Chronic Pyelonephritis	0	1	1
End Stage Renal Disease	4	0	4
Focal Segmental Glomerulosclerosis	6	3	9
HSP Nephritis	1	1	2
IgA Nephropathy	0	1	1
Inconclusive	1	2	3
Interstitial Nephritis	2	0	2
Minimal Change Disease	3	2	5
Mesangioproliferative Glomerulonephritis	48	23	71
Membranoproliferative Glomerulonephritis	24	12	36
Polycystic Kidney disease	1	0	1
Rapidly Progressive Glomerulonephritis	5	1	6
SLE Nephritis-II	4	5	9
SLE Nephritis-III	0	2	2
SLE Nephritis-IV	3	4	6
Total	102	57	159

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