Original paper

Clinicopathological Spectrum of Renal Biopsies in Children a Multicenter Study in Baghdad-Iraq

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Abstract

Background: Renal biopsy is a very important diagnostic tool for many kidney diseases which play important role in the diagnosis, management and prognosis of kidney diseases.

Aim of study: To study the indications, histopathological findings, and complications of renal biopsies in multicenter in Baghdad-Iraq.

Materials and Methods: In this retrospective and descriptive study, we included renal biopsies done in multicenter in Baghdad-Iraq, from 1st of January 2014 to 31 of December 2016, which was 120 patients up to 17 years of age

Results: Out of 120 patients, 68 cases (56.6%) were males, and 52 cases (43.3%) were females, steroid resistant nephrotic syndrome was the main indication of renal biopsy 42% followed by acute glomerulonephritis 19% and then evidence of systemic lupus erythematosus 15%, minimal change nephrotic syndrome was the most common primary kidney disease 39% followed by focal segmental glomerulosclerosis 31%. And lupus nephritis was the most common secondary kidney disease 83%, hematuria and mild pain at site of biopsy was the most common complications of renal biopsy 31.4% and 40% respectively.

Conclusion: Renal biopsy is useful in diagnosis, assess level of chronicity, management, and prognosis of kidney diseases. Steroid resistant nephrotic syndrome remain the most common indication for renal biopsy, minimal change disease and focal segmental glomerulosclerosis is the most common histopathological lesions in primary kidney diseases, lupus nephritis is the most common secondary kidney diseases. Renal biopsy under ultrasound guidance is safe with self-limited complications in form of hematuria and mild pain at site of biopsy.

Keyword: renal biopsy, Baghdad, Iraq, multi-center study

Introduction

There are two particularly important pieces of information obtained by renal biopsy [1]:

1. for diagnosis.
2. for severity and chronicity of diseases.

There are a special circumstances in each of the following headlines in which renal biopsy is indicated [2, 3].

- Hematuria
- Proteinuria
- Nephrotic Syndrome
- Acute Nephritis
- Acute Kidney Injury
- Chronic Kidney Disease
- Systemic Diseases
- Follow-Up of Disease
- Transplantation

Contraindications to percutaneous renal biopsy includes [4]:

Absolute contraindications:

- Uncontrolled coagulation abnormalities.
- Solitary kidney (not transplant)
- Acute pyelonephritis

Relative contraindications:

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- Severe azotemia/end-stage renal failure
- Anatomic abnorm
- lities of the kidney
- Coagulopathy
- Concurrent use of drugs affecting coagulation (e.g. aspirin, dipyridamole)
- Chronic pyelonephritis
- Concurrent urinary tract infection
- Tumors
- Pregnancy
- Extreme obesity

Alternatives to the percutaneous approach [6, 7]**:**

- Open renal biopsy in children.
- Laparoscopic renal biopsy.
- Aspiration Biopsy.

Complications following renal biopsy [8, 9]**:**

- Microscopic hematuria.
- Macroscopic hematuria.
- Perinephric hematoma.
- Arteriovenous fistula.
- Miscellaneous complications.

Processing and interpretation of the renal biopsy specimens [10, 11]**:**

- Light microscopy.
- Immunofluorescence.
- Electron Microscopy.
- Histopathologic Assessment.

Aim of study

1. To study the indications of renal biopsy.
2. To know the more frequent glomerular diseases according to histopathological findings of renal biopsies.
3. To assess the complications of renal biopsy.

Patients and methods

Our study was retrospective and descriptive. We included all renal biopsies performed in a three pediatric nephrology centers in Baghdad-Iraq which include central teaching hospital of pediatric, children welfare teaching hospital and Al-Karama teaching hospital from 1st of January 2014 to 31 of December 2016 in children up to 17 years of age, we exclude repeated renal biopsies, inadequate renal biopsies (<12 glomeruli), failure of renal biopsies, and deficient in clinical data.

Preparing the patient:

1. Proper history which include the history of bleeding diathesis (personal or family history), allergies to agents used during the renal biopsy, use of aspirin, nonsteroidal anti-inflammatory drugs, or other anticoagulation therapy, and a history of sever hypertension.
2. Physical examination which include blood pressure evaluation, biopsy site assessment, and assessment of anatomic abnormalities that may interfere with imaging or positioning the patient during the biopsy.
3. Laboratory evaluation which include a complete blood count, renal function test, coagulation profile, and urinalysis.
4. Ultrasonographic evaluation for any anatomical abnormality.

Procedure:

The procedure was performed after obtaining informed consent from the families of the patients. The patient is placed in a prone position with a pad under the upper part of the abdomen. The kidneys are localized by ultrasound from the back. The kidney with the lower pole that is easiest to reach, in most cases the right kidney, is then chosen for biopsy. The exact position of the kidney during inspiration is determined, and after marking the intended entry of the needle on the skin, the skin is cleaned with an antiseptic solution. At this time we give anesthesia to the patient (mostly general anesthesia and sometimes local anesthesia according to availability of general anesthesia in the center in which the biopsy was done).

All renal biopsies were performed using a percutaneous automated spring-loaded biopsy instrument (BARD 18 g×16 cm, or KIMAL 18 g×20 cm). The needle is carefully introduced under ultrasound guidance until the kidney is almost

reached. The needle is quickly advanced to the capsule of the kidney and the biopsy is taken. We take two pieces and put it in formalin solution and send the samples to a pathologist.

Post biopsy care include vital sign monitoring especially blood pressure, observation for the color of urine and sometimes hemoglobin monitoring (if the patient have a history of coagulation abnormality or hematuria post biopsy) for at least 8 hours after procedure.

In laboratory the samples were studied under light microscopy use Hematoxylin and Eosin (H & E) and Periodic Acid Schiff (PAS) stain. All the findings (regarding number of glomeruli, cellularity, interstitiam, vasculature, fibrosis, and final diagnosis) of the already stained H & E samples and immunostain study for IgG, IgA, IgM, C3, and C1q were recorded from the biopsy reports of the patients.

We study the complications of renal biopsy in only 70 patients who included in our study because that the complications in the remainder 50 patients not written in the medical records.

We defined steroid resistant nephrotic syndrome (SRNS) as a patients who fail to enter remission after 8 weeks of corticosteroid treatment [11, 12]. Steroid dependent nephrotic syndrome (SDNS) as a patients who respond to initial corticosteroid treatment by entering complete remission but develop a relapse either while still receiving steroids or within 2 weeks of discontinuation of treatment following a steroid taper [13]. Lupus nephritis was classified according to the recommendation of the International Society of Nephrology and Renal Pathology Society Working Group (ISN/RPS) revised histopathological classification of lupus nephritis [14, 15]. IgA nephropathy was classified according to Haas classification [16]. Clinical data were collected from the medical records of patients at the department of pediatric nephrology.

Statistical analysis:

All results were tabulated and calculated using the Statistical Package for the Social Sciences (SPSS) software (windows version 23.0) and the Microsoft Office Excel software 2007. Our study was descriptive and there are no any comparison between 2 groups so no need to calculate P-value.

Results

One hundred twenty patients collected from three pediatric nephrology centers in Baghdad-Iraq were included in our study.

We exclude cases of repeated renal biopsies (12 cases), inadequate renal biopsy (< 12 glomeruli) (18 cases), failure of renal biopsy (10 cases), and deficient in clinical data (8 cases).

The results in our study was as follow:

Male 68 cases (56.6%), female 52 cases (43.3%), male to female ratio 1.3:1

We divided the patients according to age into four age group, < 1 year, 1-5 years, 6-10 years, and 11-17 years.

The gender of the patients according to age group was as follow: in patients < 1 year total cases was 8, the number of males was 5 (63%) and the number of females was 3 (37%).

In patients from 1-5 years of age, total cases was 32, the number of males was 24 (75%), and the number of females was 8 (25%).

In patients from 6-10 years of age, total cases was 44, the number of males was 19 (43%), and the number of females was 25 (57%).

In patients from 11-17 years, total cases was 36, the number of males was 20 (56%), and the number of females was 16 (44%). As shown in table 1.

Indications of renal biopsy of the patients in our study was as follow:

Steroid resistant nephrotic syndrome (SRNS) 50 cases (42%), steroid dependent nephrotic syndrome (SDNS) 9 cases (7.5%), infantile nephrotic syndrome (INS) 8 cases (7%), nephrotic syndrome +

decrease complement level 3 cases, nephrotic syndrome + hepatitis B viral infection 1 case, nephrotic syndrome + age > 10 years 1 case, nephrotic syndrome (FSGS) on cyclosporine 1 case, acute glomerulonephritis (GN) 23 cases (19%), evidence of systemic lupus erythematosus (SLE) 18 cases (15%), evidence of Henoch-Shonlein nephritis (HSN) 2 case, Gross hematuria + hemoptysis 1 case, Acute decrease in GFR 2 cases, CKD of unknown cause 1 case. See table (2).

The histopathological results of renal biopsies of the patients in our study were Primary kidney diseases was 90 patients (75%) which include minimal change nephrotic syndrome (MCNS) 35 (39%), focal segmental glomerulosclerosis (FSGS) 28 (31%), IgA nephropathy (IgAN) 15 (16.6%), membranoproli-ferative glomerulonephritis (MPGN) 4 (4.4%), membranous nephropathy (MN) 2 (2%), IgM nephropathy (IgMN) 2 (2%), congenital nephrotic syndrome (CNS) Finnish type 1 (1%), diffuse mesangial sclerosis (DMS) 1 (1%), Alport syndrome 1 (1%), Goodpasture syndrome 1 (1%). See table (3).

Secondary kidney diseases according to histopathological results of renal biopsies in our study was 30 patients (25%) which include lupus nephritis (LN) 25 (83%), Henoch-Shonlein nephritis (HSN) 2 (6.6%), lysosomal storage disease 1 (3%), acute tubular necrosis 1 (3%), and cyclosporine A toxicity 1 (3%). See table (4).

Number of patients in each class of lupus nephritis (LN) according to histopathological results of renal biopsies and International Society of Nephrology and Renal Pathology Society Working Group (ISN/RPS) classification was as follow: class (I) 1 patient (4%), class (II) 15 (60%), class (III) 7 (28%), and class (IV) 2 (8%). See table (5).

We classify IgA Nephropathy (IgAN) patients according to Hass classification as follow: class (I) 2 patients (13%), class (II) 8 (53%), class (III) 4 (27%), and class (IV) 1 patient (7%). See table (6).

From 70 patients included in the study of complications of renal biopsy 22 (31.4%) suffer from gross hematuria, 28 (40%) suffer from mild pain at site of operation, 16 patients (23%) suffer from both gross hematuria and pain, and perinephric hematoma in only 1 patient, see table (7).

Table 1. Distribution of patients according to age and gender.

Age group	Male No. (%)	Female No. (%)	Total No. (%)
< 1 year	5 (63%)	3 (37%)	8 (7%)
1-5 years	24 (75%)	8 (25%)	32 (27%)
6-10 years	19 (43%)	25 (57%)	44 (37%)
11-17 years	20 (56%)	16 (44%)	36 (30%)
total	**68 (56.6%)**	**52 (43.3%)**	**120**

Table 2. Indications of renal biopsy according to age group.

Indication	< 1 year No. (%)	1-5 years No. (%)	6-10 years No. (%)	11-17 years No. (%)	Total No. (%)
SRNS	0	24 (48%)	17 (34%)	9 (18%)	**50 (42%)**
SDNS	0	2 (22%)	4 (44%)	3 (33%)	**9 (7.5%)**
INS	8 (100%)	0	0	0	**8 (7%)**
Acute GN	0	4 (17%)	12 (52%)	7 (30%)	**23 (19%)**
Evidence of SLE	0	1 (5.5%)	8 (44%)	9 (50%)	**18 (15%)**
others	0	1 (8%)	5 (42%)	6 (50%)	**12 (10%)**

Table 3. Primary kidney diseases according to histopathological results of renal biopsies.

Disease	< 1 year No. (%)	1-5 years No. (%)	6-10 years No. (%)	11-17 years No. (%)	Total No. (%)
MCNS	3 (8.5%)	16 (46%)	10 (28.5%)	6 (17%)	**35 (39%)**
FSGS	3 (11%)	9 (32%)	12 (43%)	4 (14%)	**28 (31%)**
IgAN	0	1 (6.6%)	7 (46.6%)	7 (46.6%)	**15 (16.6%)**
MPGN	0	0	2 (50%)	2 (50%)	**4 (4.4%)**
MN	0	0	0	2 (100%)	**2 (2%)**
IgMN	0	0	0	2 (100%)	**2 (2%)**
CNS Finnish	1	0	0	0	**1 (1%)**
DMS	1	0	0	0	**1 (1%)**
Alport syndrome	0	1 (100%)	0	0	**1 (1%)**
Goodpasture syndrome	0	0	0	1 (100%)	**1 (1%)**
Total	**8 (9%)**	**27 (30%)**	**31 (34%)**	**24(27%)**	**90 (75%)**

Table 4. Secondary kidney disease according to histopathological results of renal biopsies.

Disease	< 1 year No. (%)	1-5 years No. (%)	6-10 years No. (%)	11-17 years No. (%)	Total No. (%)
LN	0	2 (8%)	10 (40%)	13 (52%)	**25(83%)**
HSN	0	1 (50%)	1(50%)	0	**2(6.6%)**
Lysosomal storage dis.	0	1 (100%)	0	0	**1(3%)**
Acute tubular necrosis	0	0	1 (100%)	0	**1(3%)**
Cyclosporin toxicity	0	0	1 (100%)	0	**1(3%)**
Total	**0**	**4 (13%)**	**13 (43%)**	**13 (43%)**	**30 (25%)**

Table 5. Distribution of patients with LN according to (ISN/RPS) classification.

Class of LN	< 1 year	1-5 year	6-10 year	11-17 year	Total
Class I	0	0	1	0	**1 (4%)**
Class II	0	2	6	7	**15 (60%)**
Class III	0	0	3	4	**7 (28%)**
Class IV	0	0	0	2	**2 (8%)**
Total	**0**	**2**	**10**	**13**	**25**

Table 6. Distribution of patients with IgAN according to Haas classification.

Class of IgAN	< 1 year	1-5 years	6-10 years	11-17 years	Total
Class I	0	0	2	0	**2 (13%)**
Class II	0	1	4	3	**8 (53%)**
Class III	0	0	1	3	**4 (27%)**
Class IV	0	0	0	1	**1 (7%)**
Total	**0**	**1**	**7**	**7**	**15**

Table 7. Complications following a renal biopsy.

Adverse effect	Male No. (%)	Female No. (%)	Total No. (%)
Gross hematuria	8 (36.3%)	14 (63.6%)	**22 (31.4%)**
Mild pain	12 (43%)	16 (57%)	**28 (40%)**
Both	6 (37.5%)	10 (62.5%)	16 (23%)
Hematoma	0	1 (1.4%)	**1 (1.4%)**
No complication	11 (58%)	8 (42%)	**19 (27%)**
Total	**31 (44%)**	**39 (56%)**	**70**

Discussion

Renal biopsy is an essential diagnostic tool for histological diagnosis of glomerular and tubulo-interstitial diseases. It allows to

classify nephropathies to tailor a therapeutic approach to histopathological lesions and to assess the prognosis of the disease [17].

One hundred twenty patients included in our study from multicenter of pediatric nephrology in Baghdad-Iraq, this study provides information about patterns of renal diseases diagnosed in these centers over a period of three years.

In this study the number of males was 68 (56.6%), and the number of females was 52 (43.3%), male to female ratio was 1.3:1. This agree with another study in Morocco in which there was a slight male predominance, with a sex ratio of 1.07. This is partly due to the general masculine predominance in kidney diseases, especially in children [18, 19].

These results go with another study done in Czech Republic in 2004 include adult and children renal biopsies from 1994-2000, showed out of 710 pediatric patients, (53.2%) were males and (46.8%) were females [20].

In our study we classify the patients according to age into 4 groups which are below 1 year of age, 1-5 years of age, 6-10 years of age, and 11-17 years of age. Male to female ratio in these age groups (except age group below 1 year because limited number of cases) was 3:1, 0.8:1, and 1.25:1 respectively. We noted increase the number of females in age group 6-10 years old and proximities in the numbers of males and females in age group 11-17 years, this may be due to increase renal disease which present as a part of systemic diseases such as SLE which is more common in females.

In comparison with other study in Kanpur-India 2010, male to female ratio according age group below 5 years, 5-10 years, and above 10 years were 2.2:1, 1:1, and 2.7:1 respectively, we noted increase in the number of females after 5 years of age as in our study but return to decrease after 10 years of age [21].

The main indication for renal biopsy in our study is steroid resistant nephrotic syndrome 50 patients (42%), nephrotic syndrome was the main indication for renal biopsy in other studies in Serbia, Croatia, Jordan, and Morocco ranging from 28.5% to 63.4% of cases [18, 19, 22, & 23], while in a recent study from Hong Kong, systemic diseases were the most common indication [24].

Second indication in our study proteinuria and hematuria as a part of Acute glomerulonephritis 23 cases (19%), in other study especially in Europe and Asia hematuria was the main indication for renal biopsy [20, 25], where proteinuria was the predominant indication for renal biopsy in a British study in 2009[26], this could be related to the lack of systematic dipstick screening in children and also may be due to different renal diseases in different populations.

The 3rd indication in our study was evidence of SLE 18 cases (15%), were comparable to that reported by Printza et al. [25], while in Hong Kong study in 2008 systemic disease with renal impairment was the main indication for performing renal biopsy [24].

Primary kidney disease in our study was 90 patients (75%), and secondary nephropathy was 30 (25%), these results go with other studies (66% and 34% in Morocco, 59.8% and 25.4% in the Czech Republic, 69% and 31% in Greece, 64% and 17.3% in Serbia [18, 20, 22, & 25]. primary kidney disease was predominant among males while secondary kidney disease was predominant among females[18, 20, & 24].

Minimal change nephrotic syndrome (MCNS) was the most common histopathological results of renal biopsies in our study, these result go with other studies in Morocco, Jordan, and Pakistan [18, 19, & 27].

Focal segmental glomerulosclerosis (FSGS) was the 2nd histopathological result of renal biopsies in our study 28 patients (23%), while in other studies in Europe FSGS was the main

histopathological form in steroid resistant nephrotic syndrome followed by MCNS and mesangial cell hyperplasia [25, 28, & 29], this may be related to socio-economic states, obesity, and improved histopathological analysis.

In our study, lupus nephritis was the most common cause of secondary glomerulonephritis especially among females over 10 years of age, these results go with other studies in Morocco, Serbian, Hong Kong, and Pakistan[18, 22, 24, & 30].

Mesangial proliferative lupus nephritis (class II) was the most common histopathological form in patients diagnosed with SLE (60%), followed by focal proliferative LN (class III) (7%) regardless of disease activity, diffuse proliferative LN (class IV) only in 2 patients (8%) while in other studies class IV LN was found in approximately (20%) of children biopsied for SLE [25, 31], and (30.7%) in other study done in Morocco [18], this may be due to differences in tissue biopsy interpretation in laboratory in these studies.

IgA Nephropathy was the 3rd primary renal pathology in our study after MCNS and FSGS 15 cases (12.5%), while it was the most common cause of primary kidney disease in other studies in Europe (Spain, Italy, England) and Asia[24, 32, & 33], on the other hand, it was rare in Saudi Arabia study[34], and only 2 patients in Morocco study[18], this variation may be due to variety in race and ethnicity of the studies[25].

Seventy patients from the total number of patients in our study included in study of complications of renal biopsy because that the complications of renal biopsy in the remainder patients not written, so gross hematuria was the most important complication which occur in 22 patients (31.4%), which is resolve during several hours in majority of patients, these result go with other similar studies were hematuria following a biopsy is present in about 33.3% and 35% [21, 35].

Conclusion

1. Renal biopsy is useful for identifying the specific diagnosis, assessing the level of disease activity, and for allowing specific decision about the treatment to be used.
2. Steroid resistant nephrotic syndrome is the most common indication of renal biopsy in children while minimal change nephrotic syndrome and focal segmental glomerulosclerosis remain the most common histopathological lesions.
3. Lupus nephritis is the most common secondary kidney diseases especially in females more than 10 years of age.
4. Real-time sonographic guidance in conjugation with an automated core biopsy device is safe and accurate method in hands of trained and experienced personnel to form percutaneous renal biopsy with few complications such as hematuria which is mostly self-limited within several hours and mild pain at site of biopsy well respond to simple analgesia.

Recommendations

1. We need further studies about the pattern of biopsy-proven renal diseases including all pediatric nephrology centers in Baghdad and other Iraqi provinces for establishing a national Iraqi registry of renal biopsy in future.
2. The complication of renal biopsy should be written in medical record of the patient, abdominal ultrasound and urine analysis should be done regularly post renal biopsy procedure to detect perinephric hematoma and microscopic hematuria.
3. We suffer from a shortage in biopsy device so it should be available in sufficient amount in all nephrology centers.
4. Introduce electron microscopy as an important part of renal biopsy analysis for a more accurate diagnosis.

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