SPECTRUM OF BIOPSY-PROVEN RENAL DISEASE IN THE PEDIATRIC AGE GROUP AT KING HUSSEIN MEDICAL CENTER

Edward Saca MD, Issa Hazza MD*, Ola El-Imam MD**, Mona Kawar MD**

ABSTRACT

Objective: This is a retrospective analysis of kidney biopsies done for children with glomerular diseases in the pediatric age group.

Methods: The medical records of all children who underwent kidney biopsy between January 1999 and June 2003 were studied. Demographic data including age and gender, as well as the indication for biopsy, the result, the diagnostic value, and complications of the procedure were recorded. All biopsies were done under ultrasound guidance.

Results: A total number of 65 biopsies were done. Four were in previously diagnosed patients to rule out cyclosporine toxicity and therefore excluded from the study. The biopsy was inadequate in three cases (4.6%). All of the remaining 58 biopsies were included in the study and analyzed. The mean age at biopsy was 7.56 ± 4.22 years. Renal disease was more common in males (62.1%). The most common indication for biopsy was steroid resistant nephrotic syndrome accounting for 32.7% of the cases. The most common primary glomerular disease at renal biopsy was focal segmental glomerulosclerosis occurring in 19% of patients followed by mesangiocapillary glomerulo-nephritis and then minimal change disease. The most common secondary renal disease was Henoch - Schoenlein purpura representing 6.9% of cases followed by systemic lupus erythematosus in 3.4% of cases. The kidney biopsy was normal in 5.2% of patients.
When patients with difficult nephrotic syndrome were analyzed the most common lesion was focal segmental glomerulosclerosis in 39.1%. Mesangiocapillary glomerulonephritis was present in 26.1%, minimal change disease in 17.4%, diffuse mesangial nephritis in 13% and congenital nephrotic syndrome in 4.3%. Gross hematuria was noticed in eight (13.8%) patients; however blood transfusion was only needed in two (3.4%) patients. One patient (1.7%) required radiological intervention for AV fistula post biopsy.

Conclusion: The distribution of renal disease in the pediatric age group at King Hussein Medical Center is similar to that described in other countries with some differences. The kidney biopsy is safe and the diagnostic yield is excellent. Taking into account the lack of reliable data in Jordan this study illustrates the importance of having a regional registry for renal disease in children.

Key words: Kidney biopsy, Glomerulonephritis, Renal disease.

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Introduction

Kidney biopsy in the pediatric age group as in the adult population is one of the most important investigations in renal medicine. It identifies children with chronic glomerular diseases and has important implications on early diagnosis and therapeutic interventions. When compared with adults the rate of children undergoing kidney biopsy is not more than 10%[(1)]. Analysis of

From the Departments of:
*Pediatric, Nephrology Section, King Hussein Medical Center, (KHMC), Amman - Jordan
** Radiology, (KHMC)
Correspondence should be addressed to I. Hazza, (KHMC)
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various registries indicates that the epidemiology and spectrum of renal disease in the pediatric age group differ from one geographic place to another[2]. This illustrates the importance of establishing national registries for pediatric kidney biopsy.

Data describing the spectrum of renal disease in Jordanian children are scanty, basically due to the lack of a national registry for pediatric renal disease in Jordan. Analysis of kidney biopsies done at a single center can however give some insight to the frequencies and most significant types of glomerulonephritis encountered in this country. It can as well provide some foundation for future epidemiological analysis, and data collection.

This study describes the experience of pediatric kidney biopsy at King Hussein Medical Center in Jordan and reports on the indications, the histopathological diagnosis, and the safety of this procedure.

Procedures and methods

A retrospective analysis of the pathological reports and files of all children aged less than 14 years who underwent kidney biopsy at our center between January 1999 and June 2003 was done. A total number of 65 biopsies were done, seven biopsies (4 in previously diagnosed patients to rule out cyclosporine toxicity, and 3 termed inadequate) were excluded from the study, and 58 were subjected to analysis.

Demographic data including age and sex, as well as the indication for biopsy, the histopathological diagnosis, and the complications of the procedure were recorded. All biopsies were done under ultrasound guidance, by the pediatric nephrologist using either gun loaded or conventional true cut biopsy needle in the presence of the pediatric radiologist.

Biopsies were done under pethidine and midazolam pre-medication only; however four biopsies were done under ketamine anaesthesia which was needed in the younger age group. Two specimens were taken for light microscopy and for immunohistochemistry. Electron microscopy was not done, as the procedure was unfortunately not available in Jordan at that time.

All our biopsies were done as an in-patient procedure, as patients were observed for 24 hour after the procedure.

Indications for biopsy were grouped into five categories: nephrotic syndrome (steroid resistant and steroid dependent), non-nephrotic proteinuria, haematuria with proteinuria, recurrent gross haematuria, and the acute nephritic syndrome.

Results

The failure rate as defined by the biopsy being inadequate for histopathological diagnosis was 4.6% of the total biopsies done. The mean age at biopsy was 7.56 ± 4.22 years. Renal disease was more common in males (62.1%) than females (37.9%). The most common indication for biopsy at our center was nephrotic syndrome (Steroid resistant nephritic syndrome (SRNS) and Steroid dependant nephritic syndrome (SDNS)) accounting for 39.6% of the cases (Table I).

Table I. Indication for kidney biopsy

Indication	N	%
Nephrotic syndrome	23	39.6
SRNS	19	32.7
SDNS	4	6.9
Haematuria and proteinuria	14	24.2
Persistent non-nephrotic proteinuria	9	15.5
Recurrent gross haematuria	7	12.1
Acute nephritic syndrome	5	8.6
Total	58	100

The most common primary glomerular disease was focal segmental glomerulonephritis (FSGS) accounting for 19%, followed by mesangiocapillary glomerulonephritis (MCGN) and minimal change disease (MCD). The most common secondary renal disease was Henoch-Schonlein purpura accounting for 6.9% (Table II).

Table II. Primary versus secondary renal disease

Type	N	%
Primary glomerular disease	48	82.76
Focal segmental glomerulosclerosis	11	19.0
Mesangiocapillary glomerulonephritis	10	17.2
Minimal change disease	8	13.8
IgA Nephropathy	5	8.6
Diffuse mesangial nephritis	4	6.9
Acute proliferative glomerulonephritis	3	5.2
Membranous nephropathy	2	3.4
Tubulo-interstitial nephritis	2	3.4
Hereditary Nephritis	2	3.4
Congenital nephritic syndrome	1	1.7
Secondary glomerular disease	7	12.06
Henoch – Schoenlein purpura	4	6.9
Systemic lupus erythematosus	2	3.4
Other	1	1.7
Normal	3	5.20
Total	58	100

When patients with difficult nephrotic syndrome were analyzed separately FSGS accounted for 39.1% of cases followed by MCGN, and MCD (Table III).

Following the procedure eight (13.8%) patients developed gross haematuria, however blood transfusion was only needed in two (3.4%) patients. One (1.7%) patient, developed AV fistula malformation.

Table III. Patients with difficult nephrotic syndrome

Type	N	%
Focal segmental glomerulosclerosis	9	39.1
Mesangiocapillary glomerulonephritis	6	26.1
Minimal change disease	4	17.4
Diffuse mesangial nephritis	3	13.0
Congenital nephritic syndrome	1	4.3
Total	23	100

Discussion

This report provides some insight to the frequency of biopsy proven renal disease in the pediatric age group in Jordan. With the absence of a national registry such reports become more valuable. Although the general pattern of renal disease in Jordan matches with that reported elsewhere in developed and developing countries, there are some differences worth acknowledging.

In our report the mean age at biopsy matches that reported in various registries belonging to the developed countries[1,2-9]. Biopsy was done more frequently in males than females, which is the same as that reported elsewhere and probably reflects the fact that chronic renal disease is more common in males[2-4].

In our center the commonest indication for renal biopsy was nephrotic syndrome (steroid resistant and steroid dependent) while persistent isolated microscopic haematuria alone was not considered an indication at all. This reflects the difference in the selection criteria for kidney biopsy between centers. While it matches reports from developing countries[5-7], it does not comply with the selection criteria from developed countries, where microscopic haematuria (with or without non nephrotic range proteinuria), although still debatable is becoming the commonest indication for performing kidney biopsy[1,3,8].

The most common primary glomerular disease was FSGS, whereas IgA nephropathy, which is reported to be the commonest cause of chronic glomerulonephritis all over the world[1,8], only comprised 8.6% of cases. In the Italian national registry IgA nephropathy was the commonest primary glomerulonephritis detected at renal biopsy in children (18.8%)[1], whereas FSGS contributed to only 8.5% of biopsies[1]. This difference in frequencies is well explained by the fact that more than 50% of biopsies reported in the national Italian registry were performed for isolated microscopic haematuria and non-nephrotic proteinuria. In this group, patients with IgA nephropathy contributed to around 35% of biopsies. In our center isolated microscopic haematuria was not an indication at all for renal biopsy unless there was a family history of renal impairment and only 15.5% of all biopsies were done for non-nephrotic proteinuria. Al-Rasheed *et al*[5] reported 24% incidence of FSGS where as IgA nephropathy contributed to only 3% of biopsies done on children from Saudi Arabia, these figures are more consistent with our figures but again the indication for kidney biopsy in this study was difficult nephrotic syndrome in 77% of cases. Therefore our results as well as the results of others coming from developing countries reflect a difference in selection and indication for renal biopsy rather than a difference in frequency. We believe that the absence of electron microscopy in our center as well as in other centers in the developing world does contribute to this difference in the selection of patients undergoing this procedure. The frequency of other types of primary GN including Alport and congenital nephrotic syndrome was similar to that reported else where in the Arab world[5].

In this report there was no difference in the frequency of secondary renal disease with Henoch-Schonlein purpura being the most common as in other reports elsewhere[1,2].

Recently there have been some reports signifying the increasing incidence of FSGS as a cause of idiopathic nephrotic syndrome[10]. Kumar *et al.*[9] reported FSGS to be the most common histopathological diagnosis in biopsies from children with nephrotic syndrome, contributing to 38% of total. In this report when patients with difficult nephrotic syndrome were analysed separately FSGS was the most common cause contributing to 39.1% of cases. Diffuse mesangial nephritis contributed only to 13%, which contradicts several reports from adjacent countries concerning the higher incidence of this histopathological diagnosis in our region when compared to the western world[11].

The diagnostic yield of 95.4% in our center was somewhat lower than others, who reported a diagnostic yield exceeding 98%[12], however this could be attributed to the lack of dissecting microscope to assess for the adequacy of biopsy once it is taken. It is also noted that the number of patients who developed macroscopic haematuria was also slightly higher than other reports[12]. This can easily be explained by the fact that most of the biopsies were done using a true cut needle before the introduction of the gun loaded needle in the last 2 years of this study. One (1.7%) patient, developed persistent severe gross hematuria, that was proved by renal angiogram done one week after the procedure to be due to an AV fistula malformation. This was successfully treated by insertion of a coil in the invasive radiology department.

Conclusion

The pattern of biopsy proven pediatric renal disease is similar to that reported by countries in the same area; however there are some major differences when compared with the western world. The selection criteria for kidney biopsy in our center as it is in the whole region are very conservative, and pediatric nephrologists

are still very reluctant to do kidney biopsy for minor urinary abnormalities possibly because of lack of confidence and worries about safety. This illustrates the need for establishing new selection criteria, as early diagnosis may affect follow up and management. The importance of having electron microscopy was also illustrated as it is often the only way to diagnose some renal diseases with confidence.

The procedure was proved to be safe and the diagnostic yield was high. There is a great need to establish an in-center registry in view of the absence of national and regional registries.

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