**Kidney Biopsy Findings and Outcome in Children: Single Center Experience**

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**Abstract**

**Aim:** Kidney biopsies play a major role in diagnosing several kidney diseases. They are done for several indication. The aim of this study is to determine the spectrum of kidney diseases in Omani children less than 13 years of age that require kidney biopsy for diagnosis and the rate of complications following kidney biopsy.

**Methods:** A retrospective study of children less than 13 years who underwent a kidney biopsy over a 5-year period from January 2014 to June 2019.

**Result:** Seventy-eight children were included. The median age was 8.0 years (range 0-13 years). Minimal change disease (MCD) was the most common histopathological finding accounted for 15 (19.2%) of patients followed by lupus nephritis and focal segmental glomerulosclerosis (FSGS) in 13(16.7%) each. The most common post biopsy complication was pain required analgesia seen in 38 (49.4%) patients then gross hematuria in 10 (13%) children. No children required blood transfusion or surgical intervention in this study.

**Conclusion:** Minimal change disease (MCD) was the most common histopathological finding in our pediatric population. We did not encounter any major complications following renal biopsy procedure.

**Keywords:** Omani; Children; Kidney Biopsy; Pediatric; Lupus Nephritic; Minimal Change Disease; Focal Segmental Glomerulosclerosis.
Introduction

Many kidney diseases in children can be diagnosed and treated without a histopathological confirmation. However, in some conditions, kidney biopsy is essential to establish the diagnosis and assess the severity in order to guide management. There are several indications for kidney biopsy that include glomerular, interstitial and vascular conditions such as steroid resistant nephrotic syndrome, lupus nephritis and vasculitis. A retrospective study in Morocco showed that the most common indication for kidney biopsy in children less than 16 years of age was nephrotic syndrome with hematuria and/or renal failure(1). A systematic review of 17 studies to analyze the incidence of pediatric glomerular diseases in all Arab countries revealed that the commonest type of primary glomerular disease is minimal change disease (MCD) (29.25%), followed by focal and segmental glomerulosclerosis (FSGS) (22.34%)(2). In Oman, a study based on light microscopy and immunofluorescence to analyze the pattern of glomerular diseases conducted in a single tertiary hospital among all age groups showed that focal and segmental glomerulosclerosis (21.1%) was the most common primary glomerular disease(3). Although renal biopsies play a major role in diagnosing renal diseases, there is no study done in Oman focusing on the pediatric age group to determine the clinical indications and outcomes of renal biopsies. Our population has a high rate of consanguinity which increases the incidence of inherited kidney diseases. Moreover, with the availability of genetic testing in Oman, possibly less kidney biopsies are performed.

The aims of the study were to determine the spectrum of kidney diseases and to evaluate the outcome and complications of kidney biopsy among children less than 13 years of age in whom kidney biopsy were performed for diagnosis.

Methods

This retrospective study was conducted in the Pediatric Nephrology unit, Child Health department at Royal Hospital, one of the two tertiary hospitals in Oman preforming kidney biopsies. The study included all children bellow 13 years of age, who underwent kidney biopsy at Royal Hospital in the period between January 2014 to June 2019.

The study was approved by Royal Hospital ethical Committee.

Kidney biopsies which were done for renal masses, nephrectomies and pyeloplasties were excluded from the study. Medical record numbers (MRN) for participants were provided by the hospital information system (HIS) department. Data were collected from Al-Shifaa (an electronic clinical record system at Royal Hospital). Data collected included patient demographics, clinical finding at presentation, laboratory result, renal biopsy findings and complication followed renal biopsy. Most kidney biopsies were done under ultrasound-guidance by interventional radiologists, a few by pediatric nephrologists and only 2 (2.60%) were open biopsies that were done by pediatric surgeons. Children for kidney biopsy are admitted to the pediatric ward one day prior to the procedure, baseline laboratory work up was obtained including full blood count, renal function and electrolytes, coagulation profile and blood for crossmatch. Other laboratory investigations are requested according to the clinical condition of the child. The consent for the biopsy is taken from parents or guardians and patients are reviewed by anesthesiologist prior to the procedure. Children are kept nil per mouth as per anesthesiologist instructions. Kidney biopsies are performed under general anesthesia with real time ultrasound using GE ultrasound machine either Logic Er7 or S8 with probes either 1-5 curvilinear probe or 9 L sector probe according to the weight of the child. The biopsy is done using 18-gauge needle using manual true cut or biopsy gun (Magnum-Bard). Biopsy is obtained from the lower pole of the left kidney. The left kidney is selected due its lower position compared to the right kidney and hence easily accessible. The patient is then closely monitored after the procedure for 24 hours in the pediatric ward to observe for any complications. No patients received DDAVP (desmopressin) prior to biopsy in our cohort. It is usually given for patients who have severe renal impairment with very high urea to overcome platelets dysfunction secondary to uremia. Three core biopsies are sent to histopathology laboratory for light microscopy immunofluorescent, and electron microscopy examination. The specimen is sectioned at 4 microns thickness, processed and stained using hematoxylin, eosin, periodic acid-Schiff and methenamine silver stains. One
slide is stained for elastic Van Gieson and one for Masson trichrome. Immunofluorescence was done by direct method on frozen tissue and stained for IgG, IgA, IgM, C3, C1q, fibrinogen, kappa and lambda. Biopsies are read by one of two renal pathologists either at Royal hospital or at Sultan Qaboos university hospital. Electron microscopy is only available at Sultan Qaboos university hospital.

Data collected were entered in EpiData software. Statistical Package for the Social Sciences (SPSS) Software was used for data analysis. The frequencies and percentages of all variables were calculated.

Results

A total of 78 children were included in the study of which half were boys with a median age of 8.0 years (range from 0-13 years) on the day of biopsy. Mean weight (SD) was 25.5 kg (12.9) Patients’ demographics are shown in Table 1. Most of the patients were from Muscat and Dhofar governorates with 14 children (17.9%) from each. Two of the biopsies were done for non-Omani patients (Figure 1).

Table 1. Patient demographics.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Number</th>
<th>Percentage</th>
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<tbody>
<tr>
<td>Total</td>
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<td>100</td>
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<tr>
<td>Gender</td>
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</tr>
<tr>
<td>Male</td>
<td>39</td>
<td>50</td>
</tr>
<tr>
<td>Female</td>
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<td>50</td>
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<tr>
<td>Age in year</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 3</td>
<td>7</td>
<td>9</td>
</tr>
<tr>
<td>3 to &lt; 6</td>
<td>19</td>
<td>24.4</td>
</tr>
<tr>
<td>6 to 13</td>
<td>52</td>
<td>66.7</td>
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<tr>
<td>Mean age ±SD</td>
<td>7.28±3.35</td>
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<tr>
<td>Median age</td>
<td>8.0</td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>26</td>
<td>33.3</td>
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</table>
At presentation, 70 (89.7%) of our patients had proteinuria, 31 (39.7%) had microscopic hematuria and 12 (15.4%) had gross hematuria. Abnormal glomerular filtration rate (GFR) was found in 34 (43.6%) of patients and hypertension in 26 (33.3%) of them. Fourteen patients (17.9%) had systemic manifestations including skin rash, oral ulcers, and joint pain (Figure 2).
Seventy (89.7%) of biopsies were taken from native kidneys and 8(10.3%) were from transplanted kidneys. The indications for transplant kidney biopsy were polyoma virus (BK) viremia with allograft dysfunction in 4 patients, while the other 4 patients had allograft dysfunction with negative virology. All the renal biopsies underwent histopathological examination by light microscopy (100%). Electron microscopy report was not available for 27(34.6%) cases and the immunofluorescence was not done for 2 (2.6%) of the cases.

Minimal change disease (MCD) is the most common diagnosis revealed from renal biopsy in our patients accounted for 15 (19.2%). Followed by Lupus nephritis and focal segmental glomerulosclerosis (FSGS) the second most common finding, accounted for 13(16.7%) each. Of those with lupus nephritis, 11 were females and 2 were males. Class II lupus nephritis was seen in one patient, while class III and IV were seen in 3 and 9 patients respectively.

Hereditary nephropathy (Alport syndrome/ nephronophthisis) accounted for 10(12.8%) cases. Post infectious glomerulonephritis and thrombotic microangiopathy (TMA) accounted for 3(3.8%) each. Two of the patients with TMA were diagnosed to have atypical hemolytic uremic syndrome (aHUS) while the other patient had features of TMA in addition to chronic changes in the biopsy findings and was diagnosed to have familial FSGS. Membranoproliferative glomerulonephritis and C3 glomerulopathy were found in 2 (2.65%) while another 2 children had acute tubular necrosis. Membranous nephropathy, Finish type nephrotic syndrome, and chronic pyelonephritis accounted for 1(1.3%) each. Four of transplanted kidney biopsies were reported as Polyoma virus (BK) nephropathy, 2 as acute rejection and one each for chronic rejection and calcineurin inhibitor (CNI) toxicity. A total of 3 (3.8%) biopsies were reported as normal. The indication of kidney biopsy from these 3 patients is microscopic hematuria. Two of kidney biopsies did not have electron microscopy EM performed for them, while the third one EM sample contained only medullary tissue without glomeruli. In 4 biopsies (5.1%) the report was inconclusive or insufficient to give a diagnosis (Figure 4).
Twenty-one patients (26.9%) had genetic studies performed, one of them found to have congenital nephrotic syndrome secondary to NPHS1 mutation, 3 had familial nephrotic syndrome secondary to NPHS2 mutation and 2 had whole exome sequencing done abroad which confirmed the diagnosis of nephronophthisis.

The most common complication following renal biopsy in our patients was pain required analgesia in 38 (49.4%) followed by gross hematuria in 10 (13%) patients (Figure 4). There was no severe hematuria that required blood transfusion or surgical intervention. Arteriovenous fistula, urinomas, or death following kidney biopsy were not seen in our cohort (Figure 4). No major complications occurred after kidney biopsies done for transplant patients such as arteriovenous fistula, graft infection, or loss of graft apart from mild complication such as gross hematuria and pain which responded to analgesia. Most of these complications occurred in the first 8 hours after the procedure and the majority improved and discharged within 24 hours.
Discussion

This study, to our knowledge, is the first study in Oman that addressed kidney biopsy in children. We found that the most common diagnoses seen in kidney biopsy in our patients was minimal change disease (19.2%) followed by Lupus nephritis and FSGS (16.7%) for each. A study performed in Oman between 1999 and 2010 on the pattern of glomerular diseases based on light microscopy and Immunofluorescence for adult and pediatric patients showed that lupus nephritis was the most common glomerular disease (30.4%) followed by FSGS (21.1%) and then minimal change disease 17% (3). A retrospective study in children in Saudi Arabia found that minimal change disease was the most common histopathological finding (25%) then mesangial proliferative glomerulonephritis (15.7%) (4). A systematic review to determine the incidence of pediatric glomerular diseases in Arab world from 1990 to 2018 included 17 studies revealed that lupus nephritis comprised 36.1% of all cases, followed by minimal change disease at 29.25% then FSGS at 22.34% (2). Data from around the world showed a high prevalence of membranous-proliferative GN (MPGN) in developing areas compared to a higher prevalence of IgA-nephropathy (IgAN), and minimal change disease (MCD) in more developed countries (5). Minimal change disease is the most common histopathological diagnosis in most of the above-mentioned studies (2,4,5) and not lupus nephritis and FSGS similar to our findings. The smaller proportion of children with minimal change disease in our cohort compared to other studies may be explained by the small number of kidney biopsies that were performed in children with nephrotic syndrome as it is limited to children who have steroid resistant nephrotic syndrome or children with steroid dependent or frequent relapsing nephrotic syndrome prior to starting calcineurin inhibitor. The higher percentage of children with FSGS in our patients is possibly due to high proportion of consanguineous marriage in our population. Genetic studies for steroid resistant nephrotic syndrome were performed for 19 patients with only 4 of them found to have a genetic mutation as other genes were not tested for at our center, therefore, familial FSGS cannot be ruled out in children with negative results for NPHS1 and NPHS2 genes.

The majority of children who had kidney biopsy are above 6 year of age and that is explained by the fact that secondary renal diseases like lupus and focal segmental glomerulosclerosis due to immune dysregulation are more common in older children compared to younger children whereas we see more of congenital and hereditary renal disease which can be diagnosed by imaging and genetic studies.
Non nephrotic range proteinuria and nephrotic syndrome were the most common indication for renal biopsy in our patients which is the same finding seen in other studies (5). Studies from Turkey and Italy showed that the most frequent indication for pediatric renal biopsy was nephrotic syndrome followed by non-nephrotic range proteinuria. (7,8).

Percutaneous real-time US guided renal biopsy despite being recognized as a safe procedure in children, carries a risk of complications such as gross hematuria, perirenal hematoma, arteriovenous fistulas, infection, damage to adjacent organs, or loss of the kidney (7) Our study showed that renal biopsy is a safe procedure with a few minor complications mainly pain required analgesia and gross hematuria that did not require blood transfusion nor surgical intervention. No serious complications were seen in our cohort. We expect higher risk of complications like bleeding in children with lupus nephritis and chronic kidney disease CKD. However, in our cohort, we did not encounter major complications in these children. A study in Oman showed an incidence of complications following renal biopsy of 10% with most of them being procedure-related bleeding(10). A study from Saudi Arabia revealed similar results to ours, with severe pain at the biopsy site as the most common complication (10.2%) followed by gross hematuria (2.8%) (4).

Conclusion

Common histopathological lesions observed in our children with renal diseases is minimal change disease followed by Lupus nephritis and focal segmental glomerulosclerosis (FSGS). The main complication of kidney biopsy is pain followed by gross hematuria that did not require blood transfusion. No serious complications were seen in our cohort. The findings of this study are important for counselling children and parents prior to performing kidney biopsy.

Disclosure

The authors declared no conflict of interest

References


