Original Article

Percutaneous Kidney Biopsy and the Histopathologic Patterns of Kidney Diseases in Children: An Observational Descriptive Study at a South-East Nigerian Tertiary Hospital

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Abstract

Background: Kidney biopsy remains the best standard for kidney tissue analysis. Although percutaneous kidney biopsy is an invasive procedure, it is an indispensable part of interventional nephrology for accurate diagnosis, selection of appropriate therapy protocol, and prognostication of kidney diseases in children. With improvement in expertise among pediatric nephrologists, data on procedure outcomes are now being documented. **Aim:** We aimed to describe the outcomes in a 5-year practice of kidney biopsy at the pediatric nephrology unit in a southeast Nigerian tertiary hospital. **Patients and Methods:** An observational descriptive study conducted on the kidney biopsy performed in our facility from 2017 to 2022. The focus was on the patients' clinical profile, indications for biopsy, the adopted procedure, and the histopathologic findings. **Results:** A total of 69 patients had kidney biopsy, 40 (58.0%) were males, while 29 (42.0%) were females. Sixty-four (92.7%) patients had the procedure at the age of >10 years, while five (7.2%) at the age of <7 years. The patients' prebiopsy mean systolic and diastolic blood pressures were 111.20 ± 16.93 and 74.64 ± 12.69 mmHg, respectively. Their estimated glomerular filtration rate (eGFR) was 119.27 ± 52.78 ml/min/1.73 m^2. The most frequent indication was steroid resistance (39/69, 56.5%). Focal segmental glomerulosclerosis was the commonest histopathologic finding (38/69, 55.0%). **Conclusion:** Outcomes of percutaneous kidney biopsy at a Nigerian tertiary hospital are adjudged successful. The histopathologic patterns highlight FSGS as the major cause of steroid resistance in childhood nephrotic syndrome in this clime.

Keywords: *Childhood kidney diseases, focal segmental glomerulosclerosis, percutaneous kidney biopsy*

Introduction

Percutaneous kidney biopsy is an integral component of interventional nephrology. This invasive procedure is fundamental for the accurate diagnosis of glomerular, renovascular, and tubulointerstitial diseases, thus providing invaluable information for prognostication and patient management.[1] Despite concerns about its safety and utility in children, employing real-time ultrasound and automated biopsy needles has enhanced the success and safety of the procedure.[1] Following the introduction of ultrasonography, there has been a metamorphosis from the performance of percutaneous kidney biopsy by a nephrologist to its performance by an interventional radiologist because of the availability of the latter and the procedure-related time burden.[2] In fact, studies in developed settings indicate the same proficiency in the performance of percutaneous kidney biopsy by both nephrologists and interventional radiologists.[3-5]

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As the procedural expertise of pediatric nephrologists in several developing countries continues to improve, data on kidney biopsy outcomes and histopathologic patterns of kidney diseases are now being documented. For instance, a recent systematic review of kidney biopsies performed in low- and middle-income countries shows that procedure-associated complications in these countries were low and comparable to those in other settings.[6] Another systematic review of kidney biopsies conducted in developed settings also reported minimal complications.[7] Thus, the procedure is increasingly being performed in pediatric patients with kidney diseases because of its safety profile.

Although there is a dearth of pediatric nephrologists in sub-Saharan Africa, multicenter studies in this clime have documented changing trends in histopathologic patterns of childhood kidney diseases, such as nephrotic syndrome, based on successful renal biopsies.[8] In Nigeria, capacity training powered by the sister renal programs and fellowship training program of the International Society of Nephrology (ISN)/International Pediatric Nephrology Association (IPNA) has resulted in more numbers of pediatric nephrologists with the requisite competencies in interventional nephrology. Subsequently, several authors have reported diagnostic outcomes from the use of percutaneous kidney biopsy in Nigerian children with kidney diseases.[9-12] In southeast Nigeria, there are few reports on experiences with the procedure and the histopathologic patterns of kidney diseases. Thus, this study aims to describe the outcomes in a 5-year practice of percutaneous kidney biopsy at the pediatric nephrology unit in a southeast Nigerian tertiary hospital.

Materials and Methods

Study site

Percutaneous kidney biopsy of all patients was performed in the procedure room of the renal unit in the University of Nigeria Teaching Hospital (UNTH) Ituku-Ozalla, located at the outskirts of the Enugu metropolis. The UNTH is a tertiary hospital and a referral center established mainly for the populace domiciled in southeast Nigeria and beyond.

Renal biopsy procedure

The procedure was usually conducted in three stages: the preparation, the procedure itself, and the postprocedure care.

(1) **Preparation:** This stage involved routine preprocedure counseling on the nature, necessity, and possible complications of percutaneous renal biopsy. The patients were enrolled for the procedure either during the routine clinic visits as out-patients or during hospitalization. The international normalized ratio (INR) and/or prothrombin time (PT) and hemoglobin (Hb) level estimations, and a renal ultrasound were conducted before enlisting the patients for the procedure. Exclusion criteria were the presence of shrunken kidneys, bleeding disorders (INR >1.2), anemia (Hb <10 g/dl), anansarca, an overwhelming septicemia, and failure to obtain consent. Additionally, patients on anticoagulants or nonsteroidal anti-inflammatory drugs were excluded. The patients were often advised to fast for about 12 h before the procedure because of the need for sedation, especially in younger children in whom compliance to the procedure was a challenge.

(2) **Procedure:** An intravenous access was usually secured as the first step and 5% D/S was connected. Vital signs such as pulse rate, respiratory rate, temperature, blood pressure, and oxygen saturation were measured and documented. Random blood glucose was also measured and recorded. Children aged <12 years who were apprehensive and anxious were sedated with an intravenous midazolam at 0.1–0.2 mg/kg (but not exceeding 5 mg) and intravenous ketamine at 0.5–1 mg/kg. Both medications were diluted with water for injection and given slowly over 3–5 min. Older children who co-operated better had the procedure with the local anesthesia only, usually lignocaine. Once administered, the attending other assisting doctor monitored the patient's vital signs throughout the procedure.

All the percutaneous kidney biopsies were conducted on the left native kidneys of enlisted children. The pediatric nephrologist assisted by either a colleague or a senior resident performed it. The procedure was real-time, under ultrasound guidance with the automated spring-loaded biopsy gun. The patient was made to lie in a prone position with the abdomen resting comfortably on the sandbag and the face placed in a right lateral position. The sandbag helped to reduce the mobility of the kidneys and in lifting it up for better visibility. The health personnel involved in preparation for the procedure carried out a strict aseptic process which included a thorough hand washing, wearing of sterile gowns, facemasks, and sterile gloves. The site of the biopsy, which was at the lower pole of the left kidney, was identified with a landmark: 6 cm lateral to the spine and below the lower border of the 12th rib. The site once identified and verified with an ultrasound scan was marked first and then thoroughly cleaned with chlorhexidine antiseptic lotion (savlon), methylated spirit, and povidone iodine in that order. A drape was applied leaving only the site for the procedure accessible through a marked hole. At this time, the spring-loaded biopsy gun will be tested to confirm functionality. Through the marked biopsy site, injecting the area with 3–5 ml of lignocaine local anesthesia was performed. About 2 min later, 16-G or 18-G (depending on the age and weight of the patient)-automated biopsy gun

was gently inserted through the marked area and with the aid of an ultrasound probe advanced gently until it got to the capsule on the lower pole and 0.5 cm beyond it. The needle is quickly introduced to the capsule of the kidney and then the biopsy gun is fired.

Once a cut was made, the biopsy gun was immediately and gently withdrawn and the spring returned in order to harvest the yield. By placing sterile gauze over the site, pressure is applied to control bleeding. The specimen was carefully viewed under the hand-magnifying lens to confirm the presence of glomeruli and then gently placed in the specimen-containing bottles. A specimen was said to be adequate cut when it contained at least 10 glomeruli. Usually, this process was repeated three times (three cuts). They were correctly labeled and accompanied with a well-filled request form, quickly sent to the histopathology laboratory for further evaluation. Only light microscopy (LM) was conducted in our center, as facilities for electron microscopy (EM) or immunofluorescence (IF) were nonexistent. However, 10 patients benefitted from the H3Africa study on children with nephrotic syndrome in 2021 who, in addition to having their biopsy specimens viewed under LM, also had them examined under IF and EM.

(3) **Postbiopsy care:** The care usually began with a repeat kidney scan and vital signs within 5 min after the biopsy. Patients rested for at least 12 h while lying supine before leaving for home or returned back to the ward if on admission. An intravenous antibiotic (1 g of ampicillin/cloxacillin) was administered 6 hourly for the first 24 h to those on admission and 12 h to those on out-patient basis. This was followed by an oral co-amoxiclav given at 50 mg/kg/day twice daily for 5 days. An intravenous fluid (500 ml of 5% D/S) was also administered, followed by a liberal oral fluid intake once full consciousness was established. The applied dressing was examined for any evidence of abnormal bleeding and removed after 24 h. The patient/caregiver was informed about the possibility of change in urine color or passage of bloody urine, which would clear with time. An instruction to report back to the hospital immediately was given if any of the following complications developed: worsening of passage of bloody urine, sudden shortness of breath, dizzy or fainting spells, bleeding from the site, severe abdominal pain, or pain at the site. The patient was also advised to avoid lifting of heavy objects or strenuous activities for at least 72 h from the day of the procedure. A follow-up visit was scheduled for 2 weeks when the results were expected to be ready and available. There was a repeat biopsy for those whose reports were inconclusive.

Results

Patients' demographic, anthropometric, and clinical characteristics

Out of a total of 69 patients who had percutaneous kidney biopsy, 40 (58%) were males while 29 (42%) were females. Fifty one (73.9%) of the patients had the procedure between the ages of 10 and 14 years, while 8 (7.2%) had it between the ages of 5 and 7 years [Table 1]. The mean height (in cm) and

Table 1: Patients' demographic and clinical characteristics

Variables	*n*=69	Percent
Sex		
Male	40	58.0
Female	29	42.0
Age at diagnosis of renal disease		
<5 years	2	2.9
5–9 years	10	14.5
10–14 years	41	59.4
>14 years	16	23.2
Age at biopsy		
5–9 years	5	7.3
10–14 years	51	73.9
>14 years	13	18.8
Degree of proteinuria		
1+	14	20.3
2+	26	37.7
3+	26	37.7
4+	3	4.3

Table 2: Mean values of patients' demographic, anthropometric, and clinical profile

Variables	Minimum	Maximum	Mean	SD
Age at diagnosis (years)	3.00	18.00	12.04	3.19
Age at biopsy (years)	5.00	18.00	12.42	2.42
Sodium (mmol/l)	126.00	154.00	138.01	4.99
Potassium (mmol/l)	2.81	6.10	4.25	0.65
Chloride (mmol/l)	92.00	118.00	104.42	5.39
Bicarbonate (mmol/l)	12.00	30.00	21.01	3.79
BUN (mmol/l)	2.00	54.40	8.28	2.29
SCr (μmol/l)	32.90	1816.00	114.22	28.58
eGFR (ml/min/1.73 m^2)	4.02	276.83	119.27	52.78
Height (cm)	80.00	177.00	150.95	15.44
Weight (kg)	15.00	89.00	47.34	14.42
Systolic (mmHg)	70.00	150.00	111.20	16.93
Diastolic (mmHg)	40.00	100.00	74.64	12.69
PT (s)	9.60	16.70	13.06	1.83
INR	0.50	1.70	0.97	0.15
Biopsy throws	2.00	4.00	2.69	0.55

BUN: Blood urea nitrogen; SCr: serum creatinine; eGFR: estimated glomerular filtration rate; PT: prothrombin time; INR: international normalized ratio; SD: standard deviation

weight (in kg) were 150.95 ± 15.44 and 47.34 ± 14.42, respectively. At the time of the procedure, the mean systolic and diastolic blood pressures of the patients were 111.20 ± 16.93 and 74.64 ± 12.69, respectively. Laboratory data analysis revealed that mean Hb concentration was 10.7 ± 0.6. The mean PT (in s) was 13.06 ± 1.83, mean INR value was 0.97 ± 0.15, mean serum creatinine was 114.22 ± 28.58, and the mean eGFR was 119.27 ± 52.78 [Table 2]. As at the time of biopsy, no child was in remission. The degree of proteinuria ranged from 1+ to 4+, with 52 cases (75.4%) having either 2+ or 3+ proteinuria.

Procedure data and biopsy indications

The minimum number of throws during percutaneous renal biopsy was two, while the maximum was four. Out of the total number who had biopsy, 39 (56.5%) were children with steroid-resistant nephrotic syndrome (SRNS). Only one patient (1.4%) had the procedure due to relapse after 2 years in remission. Nine patients (14.5%) who underwent biopsy had secondary nephrotic syndrome, with six (8.7%) having lupus nephritis. As shown in Table 3, other indications for biopsy were frequent relapses/steroid dependence in steroid-sensitive nephrotic syndrome: 7 (10.1%), persistent proteinuria 1 (1.4%), persistent hematuria 1 (1.4%), rapidly progressive glomerulonephritis 2 (2.9%), and sickle-cell nephropathy 2 (2.9%).

Table 3: Indications for percutaneous renal biopsy in our series

Indications	*n*=69	Percent
Age at onset	10	14.5
FR/SD	7	10.1
Relapse after 2 years	1	1.4
SRNS	39	56.5
Persistent proteinuria	1	1.4
Persistent hematuria	1	1.4
RPGN	2	2.9
SCN	2	2.9
SLE + LN	6	8.7

FR: Frequent relapsers; SD: steroid dependence; SRNS: steroid-resistant nephrotic syndrome; RPGN: rapidly progressive glomerulonephritis; SCN: sickle-cell nephropathy; SLE: systemic lupus erythematosus; LN: lupus nephritis

Table 4: Histopathologic patterns of renal diseases in biopsied children

Histopathologic diagnosis	*n*=69	Percent
Lupus nephritis[†]		
Class III	2	2.8
Class IV	4	5.2
Steroid-resistant nephrotic syndrome		
MesPGN	11	15.9
FSGS	38	55.0
MPGN	7	10.1
Membranous nephropathy	1	1.4
Steroid-sensitive nephrotic syndrome		
MCNS	3	4.3
Inconclusive histological diagnosis	3	4.3

[†]Based on the WHO classification of lupus nephritis.
MesPGN: Mesangial proliferative glomerulonephritis, FSGS: focal segmental glomerulosclerosis, MPGN: membranoproliferative glomerulonephritis, MCNS: minimal change nephrotic syndrome

Histopathologic patterns

Focal segmental glomerulosclerosis (FSGS) was the commonest histopathologic pattern amongst patients with SRNS: observed in 38 (55.0%) of the patients [Table 4]. Membranous nephropathy was the least observed histopathologic pattern 1 (1.4%). The frequencies of other histopathologic subtypes were 3 (4.3%) for minimal change nephrotic syndrome (MCNS), 7 (10.1%) for membranoproliferative glomerulonephritis (MPGN), and 11 (15.9%) for mesangial proliferative glomerulonephritis (MesPGN). Based on the WHO classification for lupus nephritis, Class III histopathologic type was seen in two (2.8%) of the patients, while four (5.7%) exhibited Class IV type. Inconclusive histopathologic report was noted in three (4.3%) of the patients.

Discussion

Percutaneous renal biopsy remains an important clinical procedure that aids in the diagnosis of kidney pathology, thus making establishment of appropriate management possible. With improved expertise in the procedure in our setting, we sought to report our 5-year experience of kidney biopsy in children and discuss the outcomes, especially the histopathologic patterns of kidney diseases.

In this study, there was a male preponderance among the pediatric patients that had the procedure. We suggest that this sex disparity in our patients may be related to the fact that majority of them had nephrotic syndrome, a kidney disease widely reported to be commoner in males.[13-17] Also, SRNS of the nonminimal change pattern was the commonest indication for kidney biopsy in our series, and its usefulness in such cases cannot be overemphasized. Given that proteinuria is a risk factor for progression to kidney failure in patients with SRNS,[18-21] it is critical to establish a histopathologic diagnosis and justify the commencement of other immunosuppressive drugs (such as calcineurin inhibitors) to achieve full or partial remission: thus halting or delaying progression to chronic kidney disease stage 5.

Interestingly, our study has revealed that FSGS is the commonest histopathologic subtype associated with SRNS in childhood. The rising prevalence of FSGS had previously been reported in our center.[22] This finding agrees with those of other studies in other parts of Nigeria[9,10,12,23] and in some sub-Sahara African countries.[24,25] More importantly, a similar trend had been reported in Saudi Arabia,[26] in Asian countries,[27,28] and in some Western countries.[29,30] Hitherto, MCNS was presumed to be the predominant histopathologic variant in pre-adolescent children in the Western world,[31] and even globally.[32] However, a recent study in Europe suggests a high prevalence rate of FSGS, with almost the same prevalence rate as MCNS.[33] Some reasons have been advanced to explain this trend toward FSGS. First, both FSGS and MCNS are considered to represent the extreme ends of the same disease spectrum given the fact that their EM findings are similar although their LM findings differ.[34] Second, the improved expertise in percutaneous kidney biopsy leading to a large glomerular yield and targeting of deep juxtamedullary glomeruli at each throw means an increased likelihood of a histopathologic diagnosis of FSGS; on the other hand, the diagnosis is most likely to be missed if only cortical glomeruli were to be biopsied.[32,35-37]

Furthermore, our study showed that MPGN and MesPGN were the next predominant histopathologic subtypes associated with SRNS in our pediatric patients. This observation is consistent with the reports of other authors in southwest Nigeria,[9,23,38] northwest Nigeria,[10] and South Africa.[25] Specifically, MesPGN was listed as one of the major histopathologic types in two studies,[23,25] whereas MPGN was the most frequent histopathologic pattern in two southwest Nigerian studies[23,39] and was listed as a prominent pattern in other studies.[9,10,38] In contrast, the incidence of idiopathic MPGN appears to be the least common histopathologic pattern in developed countries.[40] Importantly, it is associated with a very high rate of steroid resistance in comparison with FSGS.[31] Generally, there is a global increase in the prevalence rate of FSGS when compared with the rates of other histopathologic subtypes. In fact, the transition trajectory of the most frequent histopathologic pattern in Nigeria has evolved from quartan malaria nephropathy in the 1960s to MPGN in the 1980s and to FSGS till date.[9]

Again, our experience with percutaneous kidney biopsy in children threw up three major challenges. First, it was difficult obtaining consent as many patients and caregivers rejected the procedure out rightly out of fear and sociocultural/religious beliefs. The second challenge was that of cost. Currently, the country's National Health Insurance Scheme does not fund the procedure. Thus, caregivers usually paid out-of-pocket to fund the procedure. Nevertheless, 10 of the children enlisted for the procedure benefitted from H3Africa project: hence, the caregivers made no expenditure. Third, lack of facilities for IF and EM of biopsied renal tissues (except in the few who benefitted from the H3Africa project) did not allow for complete and comprehensive histopathologic diagnosis.

Conclusions

Outcomes of percutaneous kidney biopsy at our center are adjudged successful. The histopathologic patterns highlight FSGS as the major cause of steroid resistance in childhood nephrotic syndrome in this clime. With minimal complications, precise histopathologic diagnosis, and institution of appropriate management, kidney biopsy is an essential component of pediatric nephrology practice. Acquisition of competencies in this procedure would improve the practice of nephrology in these settings.

Ethics approval

This study was conducted retrospectively from data obtained for clinical purposes. Data obtained were anonymized; hence, an expedited ethical clearance was obtained from the Health Research and Ethics Committee (HREC) of the UNTH, Ituku-Ozalla, Enugu, with an approval number: UNTH/HREC/2022/10/487). Also, all experimental protocols were approved by the HREC of the hospital who also waived the need for informed consent as data were collected from the case files. All methods were carried out in accordance with relevant guidelines and regulations.

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We also acknowledge H3Africa Kidney Disease Research Network for sponsoring 10 patients and conducting IM and EM and ribonucleic acid studies as we do not have these facilities.

Consent to participate

The HREC of the University of Nigeria Teaching Hospital waived the need for informed consent as data were collected from the case files.

Availability of data and materials

The datasets generated and/or analyzed during the current study are not publicly available due to risk of data breach and the hospital policy that does not support data resharing but are available from the corresponding author on reasonable request.

Author contributions

All authors contributed to the study conception and design. Material preparation, data collection, and analysis were performed by Ngozi R. Mbanefo, Samuel N. Uwaezuoke, Ugo N. Chikani, and Adaobi I. Bisi-Onyemaechi. The first draft of the manuscript was written by Ngozi R. Mbanefo and Samuel N. Uwaezuoke and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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