



THE INDICATIONS, HISTOLOGICAL PROFILE AND COMPLICATIONS OF PERCUTANEOUS KIDNEY BIOPSY AT A NIGERIAN HOSPITAL: A 5-YEAR RETROSPECTIVE ANALYSIS

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Abstract

Background: Percutaneous kidney biopsy is a critical diagnostic procedure that provides essential insights into kidney disease aetiology and informs treatment strategies. In Nigeria, where kidney disease prevalence is high, understanding the indications, histological findings, and complications of biopsies is vital for enhancing patient outcomes.

Aim: This study evaluated the techniques employed at Zenith Medical and Kidney Center, Abuja; the indications for native and allograft kidney biopsies; procedural complications; histological yield (nephrons per biopsy); and the most common histological diagnoses.

Methods: A retrospective analysis was conducted on all patients who underwent ultrasound-guided percutaneous kidney biopsies at Zenith Medical and Kidney Center from January 1, 2018, to December 31, 2023. Data were extracted from patients' electronic medical records and histology reports.

Results: The study included 110 patients who underwent 111 biopsies (51 native and 60 allograft). Ultrasound-guided procedures were performed in 109 patients (98.2%), while 2 had open biopsies. The predominant indication for native biopsies was persistent proteinuria (74.5%), while chronic allograft dysfunction was most common for allograft biopsies (58.3%). Histological analysis was diagnostic in 88.3% of cases. Primary kidney diseases were identified in 25 (49%) native kidney biopsies, with focal segmental glomerulosclerosis (FSGS) being the most frequent (19.6%). In allograft biopsies, chronic active antibody-mediated rejection was the most common finding (50.1%). Minor complications occurred in 5 (4.5%) patients, while major complications necessitating nephrectomy occurred in 2 (1.8%) patients.

Conclusion: Ultrasound-guided percutaneous kidney biopsy at Zenith Medical and Kidney Center is safe and effective, yielding histological results that meet international standards and significantly enhancing patient care.

Keywords: Percutaneous, Kidney biopsy, Ultrasound-guided, Allograft, Histology.

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INTRODUCTION

Percutaneous kidney biopsy is a crucial diagnostic procedure utilized in the assessment of various kidney diseases. It is a very important aspect of clinical and interventional nephrology. Kidney biopsy was first introduced to clinical medicine in 1944 and later in 1951 by Iversen and Brun and has since provided clinicians with crucial information about kidney disease and optimal line of management.¹ The kidney biopsy procedure has evolved significantly since its inception, with advancements in real-time imaging technology and biopsy techniques increasing its safety and diagnostic utility.²

Although biopsies in native and allograft kidneys aim to obtain tissue for histopathological evaluation, there are significant differences in their indications, techniques and histological interpretation.³ Native kidney biopsies are typically indicated in patients with unexplained persistent proteinuria, haematuria, and acute or chronic kidney disease. It is often performed under ultrasound guidance, targeting the inferior pole of the kidney to avoid injury to surrounding blood vessels.^{2,3} It is usually done in the prone position and can be technically more challenging due to the deeper anatomical position of the native kidneys. The primary focus in the histological analysis of native kidney tissue is the detection of primary and secondary glomerular disease, standard stains such as haematoxylin and eosin, periodic acid-schiff and silver methenamine stains are used in combination with immunohistochemistry, immunofluorescence and/or electron microscopy.^{2,3}

In contrast, allograft biopsies are conducted frequently for both diagnostic and surveillance purposes.⁴ Beyond allograft dysfunction, protocol biopsies can also be scheduled at predefined intervals post-transplantation as part of routine monitoring.^{4,5} This practice is used to detect subclinical rejection, allowing for early intervention to improve graft survival.⁵ Kidney allografts are usually located extraperitoneally in the iliac fossa, hence the biopsy is done in the supine position and this superficial anatomical location also makes the procedure technically easier and safer.⁴ Analysis of allograft kidney tissue is often focused on identifying features of rejection, drug toxicity and

chronic allograft injury.⁴ In addition to standard staining techniques, C4d staining and staining for viral antigens are also crucial aspects of allograft tissue analysis.^{4,6} The Banff classification system, which was first introduced in 1991 but has undergone several revisions since, provides standardized criteria for interpreting allograft biopsy findings and plays a crucial role in guiding treatment protocols.⁶

Despite the significant prevalence of kidney disease in Nigeria, there is limited data on the histological profile of kidney biopsies especially for allograft kidney biopsies. Zenith Medical and Kidney Centre being a transplant centre and an International Society of Nephrology (ISN) training centre in interventional nephrology is now increasingly performing this important procedure to better guide patient care. This retrospective analysis over a 5-year period was aimed at evaluating the histological yield, indications and associated complications of percutaneous kidney biopsies conducted in the facility. Examining the outcomes of these biopsies would provide insights into the diagnostic efficacy, disease spectrum and safety profile of the procedure. Understanding these aspects is essential for optimizing patient management and improving the clinical outcomes of individuals with kidney pathology.

Materials and Methods

This was a retrospective analysis of all patients (110) who underwent an ultrasound-guided percutaneous kidney biopsy at Zenith Medical and Kidney Center, Abuja over a 5-year period spanning from 1st January 2018 - 31st December 2023. The electronic medical records of the patients were reviewed and the following data were extracted; sociodemographic characteristics, indication for biopsy, adequacy of biopsy sample, number of glomeruli per core, complications and histological diagnosis.

The hospital is a 120-bedded facility with an average of 800 admissions per year and a high turnover rate. It is accredited to provide training in Internal medicine and Nephrology subspecialty for resident doctors. The hospital performs an average of 14 living-donor kidney transplants every month and receives patients from different parts of the country.



Regarding immunosuppressive protocol for transplant recipients, all receive induction therapy with intravenous rabbit anti-thymocyte globulin (1 mg/kg) and methylprednisolone 500 mg/day on days 0, 1 and 2. Subsequently, they are commenced on triple maintenance immunosuppression with tacrolimus (0.1mg/kg in 2 divided doses), mycophenolate mofetil (1g twice daily) or mycophenolate sodium (720 mg twice daily) and oral prednisolone (40mg daily for 1 week and tapered by 10mg weekly until 10mg daily). Tacrolimus levels are measured for every recipient on postoperative day 6, then repeated as indicated based on its level and patients' clinical state in the early postoperative period. For stable patients, tacrolimus assays are done every 2 months. In patients that have intolerable adverse effects to the above regimen, cyclosporine or sirolimus may be substituted and drug levels for these medications are also monitored regularly

The kidney biopsies were performed by the Nephrologists in the hospital and assisted by resident doctors. All biopsies were done after getting informed consent from the patients. They were performed on both outpatient and inpatient basis as indicated. Baseline coagulation profile, full blood count, electrolytes, urea and creatinine were obtained from all patients. Exclusion criteria for the kidney biopsy included abnormal coagulation profile, low haemoglobin levels < 9g/dl, elevated creatine levels > 600µmo/l, uncontrolled hypertension, active sepsis, low platelets < 90,000 cells/mm³ and uncooperative patients. Antiplatelet therapy was discontinued 1 week before the biopsy. Outpatients presented on the day of the procedure. An intravenous access was established, and they were taken to a dedicated comfortable room in the facility. Real-time ultrasonography guidance with a convex × 3.5 MHz transducer (General Electric Logic-e) was used throughout the procedure for all patients.

Concerning native kidney biopsies, patients were placed in the prone position with a pillow placed firmly underneath the abdomen. Ultrasound was conducted to measure the kidney sizes and the depth from the skin to the kidney capsule. The lower pole of the left kidney is identified (most commonly used) unless contraindicated necessitating taking the biopsy from the right kidney. The site was cleaned with

antiseptic solution and methylated spirit and a drape was placed over it. About 10mls of 1% lidocaine was administered using a size 16-gauge cannula to anaesthetize the skin down to the kidney capsule. A 16-gauge semi-automated spring-loaded disposable core biopsy needle with a 22mm sample length (Bard Monopty gun, C. R. Bard Inc., Arizona, USA) was used to obtain kidney tissue in all biopsies; this was advanced under real-time ultrasonography into the kidney cortex and a minimum of two tissue cores were taken. Each biopsy specimen was transported in 10% buffered formalin solution and Michel's solution for analysis in the pathology laboratory.

Concerning allograft biopsies, patients were placed in the supine position. The site, typically the right iliac fossa, was cleaned with antiseptic solution and methylated spirit. A drape was applied over the cleaned area. The upper pole of the allograft kidney was identified with the allograft kidney size measured and depth from the skin to the cortex determined with ultrasound. About 5mls of 1% lidocaine was used in infiltrating from the skin to the kidney capsule. A 16-gauge semi-automated spring-loaded disposable core biopsy needle with a 22mm sample length (Bard Monopty gun, C. R. Bard Inc., Arizona, USA) was used to obtain the kidney tissue. The biopsy gun was advanced under real-time ultrasonography into the cortex to the predetermined depth and a minimum of two tissue cores were taken. Each biopsy specimen was transported in 10% buffered formalin solution and Michel's solution for analysis in the pathology laboratory.

After the procedure, a firm occlusive dressing was placed at the biopsy site and the patients were made to lie on their backs for about 4 - 6 hours. Intravenous analgesics and 500mls of intravenous fluid (0.9% saline) were administered during the observation period with serial monitoring of vital signs and urinalysis. Light microscopy, immunofluorescence or immunohistochemistry were performed on all samples. For patients who had allograft nephrectomies, the allograft was transported en bloc in 10% buffered formalin solution to the pathology laboratory where representative histological samples were taken and analyzed.



Categorical variables were analyzed as proportions while quantitative data were expressed as means \pm standard deviation and presented as tables and charts. Data analysis was carried out using the SPSS version 28.0 for Windows (SPSS Inc., Chicago, USA).

Operational terms:

Persistent proteinuria: presence of unexplained proteinuria of $>1\text{g/day}$ on 24-hour urinary protein excretion or urinary protein-creatinine ratio of 1g/g for ≥ 6 weeks.

Nephrotic-range proteinuria: 24-hour urinary excretion of $\geq 3.5\text{g}$ or urinary protein-creatinine ratio of $\geq 3.5\text{g/g}$ in a spot urine sample with or without oedema.²

Unexplained Acute Kidney Injury (AKI): increase in serum creatinine by $> 0.3\text{mg/dl}$ ($> 26.6\mu\text{mol/l}$) within 48 hours or presumed to have occurred within the preceding 7 days; or urine volume $< 0.5\text{ml/kg/h}$ for 6 hours without a known aetiology.⁷

Unexplained chronic kidney disease: irreversible decline in kidney function persistent for ≥ 3 months with no apparent aetiology and normal sized kidneys.⁷

Allograft dysfunction: defined as a rise in baseline serum creatinine by 25% or more and/or the presence of persistent proteinuria or sudden decline in urine output following a period of stable graft function. This is further categorized into immediate (< 1 week post-transplantation), early (1 week - 3 months post-transplantation) and late (> 3 months post-transplantation).^{8,9}

Adequate biopsy sample: defined as one in which the Nephropathologist was able to make a histological diagnosis, and it usually included a minimum of 5 glomeruli for suspected glomerular lesions, 5 - 10 glomeruli for tubulointerstitial disease in native kidney biopsy samples and ≥ 7 glomeruli in an allograft biopsy sample.²

Major complications: defined as the need for blood transfusions, surgical interventions and extended hospitalization post-biopsy.

Minor complications: defined as haematuria requiring no interventions and post-biopsy pain.

RESULTS

In the study period, one hundred and eleven (111) biopsies; consisting of 51 native biopsies and 60 allograft kidney biopsies were conducted amongst one hundred and ten (110) adult patients with one repeat native kidney biopsy. The commonest indication for native kidney biopsy was unexplained proteinuria while for allograft kidney biopsy, the primary indication was late allograft dysfunction (suspected chronic rejection). The indications for native and allograft kidney biopsies in this review are outlined in Tables 1 and 2.

Table 1. Indications for Native Kidney Biopsy

Indication	Frequency (n) N = 51	Percentage (%)
Unexplained persistent proteinuria	28	54.9%
Nephrotic-range proteinuria	10	19.6 %
Unexplained acute kidney injury	3	5.9%
Unexplained chronic kidney disease	5	9.8%
Systemic diseases with renal involvement	5	9.8%

Table 2. Indications for Allograft Kidney Biopsy

Indication	Frequency (n)	Percentage (%)
N = 60		
Immediate allograft dysfunction (sudden decline in urine output)		
<ul style="list-style-type: none"> Suspected acute rejection Suspected acute tubular necrosis (ischaemic-reperfusion injury) 	3	5%
Early allograft dysfunction (≥ 25% increase in baseline serum creatinine)		
<ul style="list-style-type: none"> Suspected acute rejection Suspected BK-virus-associated nephropathy Suspected calcineurin inhibitor toxicity Suspected chronic antibody-mediated rejection 	13	21.7%
	3	5%
	3	5%
	35	58.3%

Percutaneous kidney biopsy was conducted in the majority of cases (98.2%) while biopsy samples were taken following allograft nephrectomies in 2 patients (1.8%). Adequate tissue samples were obtained in ninety-eight (98) of the biopsies giving a diagnostic yield of 88.3%.

In the remaining 12.7%, histology either revealed no significant pathology (10%) or non-kidney tissue (2.7%).

Histological diagnosis was attained in 43 of the 51 native kidney biopsies. The commonest primary histological diagnosis in the native kidney biopsies was focal-segmental glomerulosclerosis, found in 10 patients (19.6%), followed by minimal change disease and membranoproliferative glomerulonephritis, each present in 9.8% of cases. The most prevalent secondary histological diagnosis was lupus nephritis (9.8%) while there was a single case of renal amyloidosis (2%). Figure 1 illustrates the various histological diagnoses in the native kidney biopsies.

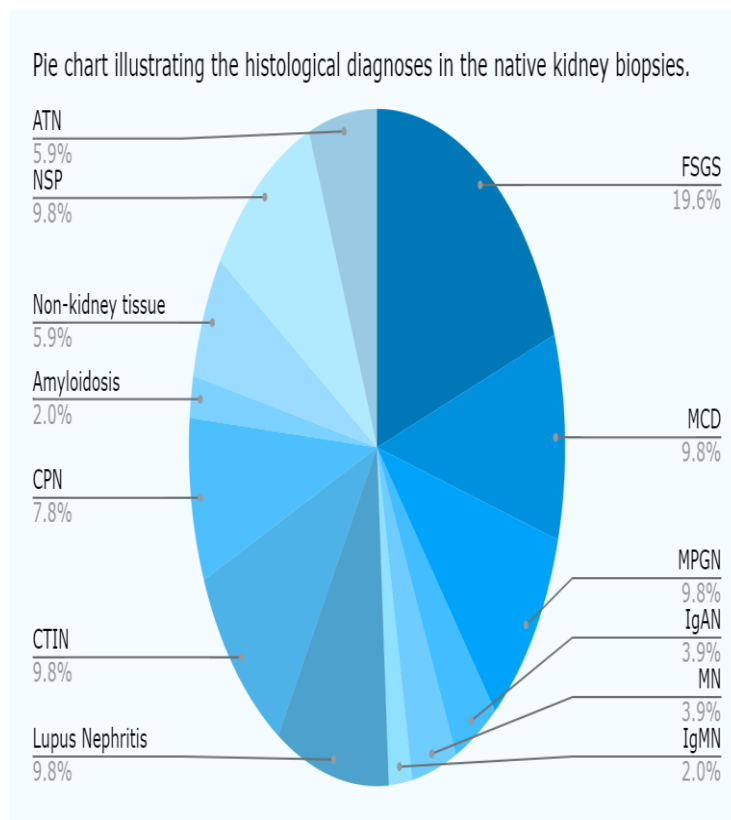


Figure 1. Histological profile of the native kidney biopsies.

ATN: acute tubular necrosis; CPN: chronic pyelonephritis; CTIN: chronic tubulointerstitial nephritis; FSGS: focal-segmental glomerulosclerosis; IgAN: IgA nephropathy; IgMN: IgM nephropathy; MCD: minimal change disease; MN: membranoproliferative glomerulonephritis; MPGN: membranoproliferative glomerulonephritis; NSP: no significant pathology

The histological findings in the allograft kidney biopsies are depicted in Figure 2. Chronic active antibody-mediated rejection was the commonest finding, present in 50% of the cases. Acute T-cell mediated rejection; a common cause of early allograft dysfunction was present in 10 patients (16.7%). Chronic tubulointerstitial nephritis was found in 5 patients while in another 5 (8.3%), no significant pathology was reported.

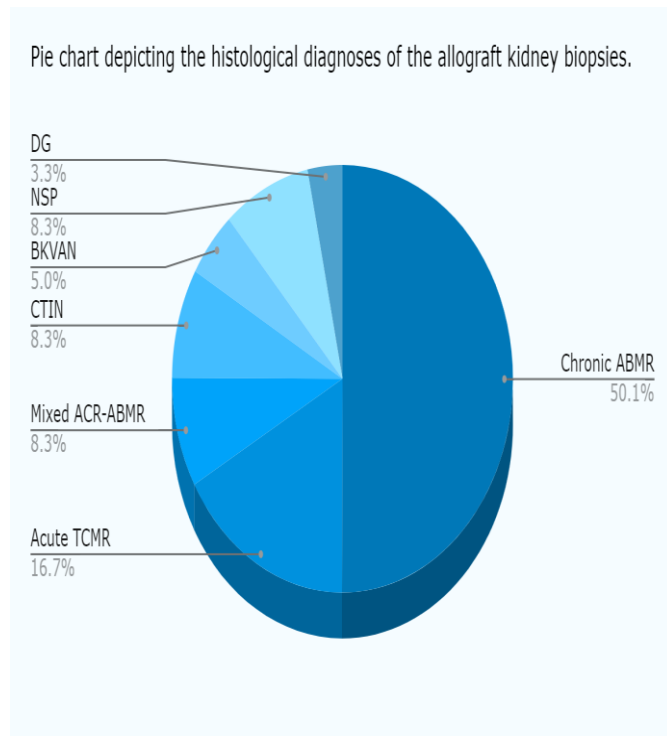


Figure 2. Histological profile of the allograft kidney biopsies.

ABMR: antibody-mediated rejection; ACR-ABMR: acute cellular rejection-antibody mediated rejection; BKVAN: BK-virus associated nephropathy; CTIN: chronic tubulointerstitial nephritis; DG: diffuse glomerulosclerosis; NSP: no significant pathology

In the majority of cases (95.5%), the biopsy procedure was well tolerated and complications-free. Minor complications were documented in 5 (4.5%) of the patients. In 2 patients, major complications occurred (i.e. gross haematuria) requiring blood transfusions, nephrectomy and increased hospital stay.

DISCUSSION

The routine practice of kidney biopsy is under-utilized and often under-reported in many developing countries within Sub-Saharan Africa, primarily due to a shortage of skilled nephropathologists, the unavailability of electron microscopes and limitations in specialized staining techniques particularly immunofluorescence staining, alongside the high cost of the procedure.¹⁰⁻¹² This review presents our 5-year experience with kidney biopsies during which we conducted 111 biopsies (51 native and 60 allograft kidney biopsies) among 110 patients (with one repeat native biopsy). This distribution is expected, given that our facility is a transplant centre. To the best of the researchers' knowledge, this represents the highest number of reported allograft biopsies in the country.

The primary indication for native kidney biopsy in this cohort was unexplained proteinuria, encompassing both nephrotic-range and sub-nephrotic-range proteinuria, which accounted for 74.5% of cases. This finding aligns with reports from multiple centres, both locally and internationally, where nephrotic syndrome is identified as the most frequent indication for kidney biopsies.¹³⁻¹⁷ Additionally, unresolved acute kidney injury (AKI) was noted as an indication in 3 (5.9%) patients, with all three ultimately diagnosed with acute tubular necrosis, underscoring the diagnostic and prognostic value of kidney biopsies. A European study corroborates this, revealing that the insights gained from biopsy reports led to therapeutic modifications in over 70% of cases.¹⁷ The remaining indications included unexplained chronic kidney disease and systemic disease with renal involvement.

In this review, the majority of allograft biopsies were conducted as a result of chronic allograft dysfunction which often presented with an asymptomatic rise in creatinine or persistent proteinuria, this was found in 35 of the 60 allograft biopsies, representing 58.3%. Allograft dysfunction in the immediate and early post-transplant period presenting with a sudden decline in urine output or worsening renal function, often with a clinical suspicion of acute rejection accounted for the remaining indications for allograft biopsy, in 10% and 31.7% respectively. This is in



contrast to the report by Gaur *et al.* which reported acute allograft dysfunction as the commonest indication for allograft biopsy, present in 54% of cases compared to chronic allograft dysfunction which was present in 28.66% of their cohort.¹⁸ The transplant recipients in this review all underwent living-donor kidney transplantation, this factor, in addition to advancements in immunosuppressive therapy which has led to an improvement in short-term outcomes in transplant recipients may be responsible for this difference.¹⁹

Imaging guidance is the gold standard when conducting kidney biopsies, it improves the safety and diagnostic yield of the procedure.¹⁷ The majority of biopsies were performed percutaneously under ultrasound scan (USS) guidance, with only 2 patients undergoing open biopsies during allograft nephrectomies. We reported a diagnostic yield of 88.3% and over 90% of the tissue samples had greater than 5 nephrons. The diagnostic yield of kidney tissue samples correlates positively with the number of visualized glomeruli, though a minimum of five glomeruli is required for the accurate diagnosis of glomerular disease.^{2,17} The adequacy of kidney tissue samples is also influenced by the gauge of the biopsy needle used. In their study, Roth *et al.* demonstrated that the use of smaller gauge biopsy needles (> size 18-gauge) while resulting in lower complications, often led to insufficient tissue samples for appropriate diagnosis and an increased need for re-sampling.²⁰ A size 16-gauge biopsy needle was used in this study.

In this study, focal segmental glomerulosclerosis (FSGS) was the most frequent (19.6%) primary histological diagnosis among native kidney biopsies. This is in agreement with data from previous studies which have demonstrated a high prevalence of FSGS amongst patients of African descent.

This has been linked to a combination of genetic and environmental susceptibility factors such as apolipoprotein-1 (APOL-1) gene polymorphisms and chronic infections.^{10,12,21} This was however in contrast to the findings of a 10-year review by Onwubuya *et al.* where membranoproliferative glomerulonephritis (MPGN) and minimal change disease (MCD) were the predominant

primary glomerulopathies, although this difference could be explained by the higher proportion of paediatric-aged cohort in their study population.¹¹ Additionally, we identified a few cases of membranous nephropathy (3.9%), IgA nephropathy (3.9%) and IgM nephropathy (2%) which were still amenable to definitive treatment highlighting the therapeutic import of reaching a definitive diagnosis with histological analysis.

A single case of renal amyloidosis was documented in this study however, lupus nephritis was the most prevalent cause of secondary glomerulonephritis, consistent with findings from other reports across Sub-Saharan Africa, Asia and Europe.^{12,14,15} Given the high prevalence of chronic ingestion of herbal remedies and non-steroidal anti-inflammatory drugs in our region, approximately 1 in 10 of the patients in this study had chronic tubulointerstitial nephritis (CTIN).¹⁰⁻¹²

Among allograft kidney biopsies, the most common histopathological diagnosis, in descending order of frequency was chronic antibody-mediated rejection (ABMR) (50.1%), acute T-cell mediated rejection (TCMR) (16.7%), mixed acute cellular rejection-antibody mediated rejection (8.3%), CTIN (8.3%), BK virus-associated nephropathy (5.0%) and diffuse glomerulosclerosis (3.3%). No specific pathology was identified in 8.3% of cases. It is well documented that there is a time-dependent pattern to the aetiology and histological findings in allograft dysfunction and this may explain the high prevalence of chronic ABMR in our study as most of the affected transplant recipients presented more than 1 year post-transplantation.^{9,22,23} Furthermore, the high cost of immunosuppressive therapy, typically borne entirely by the patients, contributes to poor medication adherence, which may promote the development of de-novo antibodies.^{9,22-24} The predominance of chronic ABMR observed in this study is consistent with findings reported by Sellares' *et al.* in the United States and Redondo-Pachón *et al.* in Spain.^{25,26} In contrast, a recent report from Pakistan found that mixed lesions were more prevalent in their study cohort, a finding attributed to delays in performing allograft biopsies.²⁷



Although percutaneous kidney biopsy is a valuable diagnostic procedure, it carries inherent risks.^{16,17} The major factors influencing complication rates include inadequate pre-procedural patient preparation, patient gender, biopsy technique (blind vs image-guided), biopsy needle type and size, the presence of comorbidities, hospitalization status and elevated baseline serum creatinine levels (> 2 mg/dl).¹⁶ In a recent systematic review, Kajawo *et al.* reported complication rates of 24.5%, 14.9% and 12.4% for kidney biopsies performed blindly, with ultrasound pre-marking and with real-time ultrasound guidance, respectively.²⁸ Similarly, in the United States, Corapi *et al.* in a meta-analysis of 34 studies involving over 9000 biopsies, demonstrated a significantly higher rate of blood transfusions associated with the use of 14-gauge biopsy needles compared to smaller gauge needles (2.1% vs 0.5%, $p = 0.05$).²⁹ The overall complication rate reported in this review was relatively low at 4.5%, which is lower than the 14.9% overall complication rate documented in a recent systematic review of 39 studies conducted in 18 low- to middle-income countries.²⁸ Major complications, specifically significant haemorrhage requiring nephrectomy occurred in 2 (1.8%) patients which is comparable to the 1.6% major complication rate reported in the aforementioned systematic review.²⁸ This lower complication rate may be attributed to the utilization of real-time ultrasound guidance, the employment of a 16-gauge automated biopsy gun, and the experience of the Nephrologists performing the procedures.

CONCLUSION

This review offers a unique perspective on the pathological diagnoses of both native and allograft kidney biopsies in a Nigerian facility. It represents one of the largest studies on allograft biopsies in Nigeria, providing valuable insights into the major causes of allograft dysfunction in transplant recipients. Additionally, it corroborates previous findings regarding the histopathological profile of native kidney biopsies. The findings from this review contribute to the growing body of evidence in the region and may help drive the establishment of a national database to inform future

research and facilitate the development of evidence-based treatment guidelines.

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