BIOMEDICINE AND CHEMICAL SCIENCES
AN INTERNATIONAL PEER-REVIEWED JOURNAL

BIOMEDICINE AND CHEMICAL SCIENCES
Website: https://journals.irapa.org/index.php/BCS
e-ISSN: 2790-296X | p-ISSN:2957-5826

Original Article

Histopathological Evaluation of Renal Biopsies: A Five-Year Retrospective Study

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Article History:
Received on: Aug 03, 2026
Revised on: Aug 10, 2026
Accepted on: Aug 20, 2026
Published on: Sep 01, 2026

Citation: Dr. Sylvester Noeldoss Lazarus *et al.* Histopathological Evaluation of Renal Biopsies: A Five-Year Retrospective Study. *Biomedicine and Chemical Sciences, 5 (3): 21-25, 2026*

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ABSTRACT

Background: Renal biopsy provides decisive diagnostic and prognostic information in medical renal disease, particularly when clinical and laboratory findings overlap.

Materials and methods: This five-year retrospective study evaluated the histopathological spectrum of native renal biopsies received in a tertiary care center. Records of 312 adequate native kidney biopsies were reviewed for age, sex, clinical indication, light microscopic diagnosis, immunofluorescence pattern and chronicity features.

Results: The mean age was 34.9 +/- 16.8 years, and 54.8% were male. Nephrotic syndrome was the commonest indication (42.6%), followed by nephritic syndrome (18.9%), asymptomatic urinary abnormalities (14.1%), acute kidney injury (12.2%) and systemic disease evaluation (12.2%). Primary glomerular diseases constituted 198 cases (63.5%), secondary glomerular diseases 72 cases (23.1%), tubulointerstitial diseases 24 cases (7.7%) and vascular/chronic sclerosing lesions 18 cases (5.8%). Focal segmental glomerulosclerosis was the most frequent diagnosis (19.2%), followed by IgA nephropathy (14.4%), membranous nephropathy (11.2%) and lupus nephritis (13.1%). Interstitial fibrosis/tubular atrophy >25% was significantly associated with reduced estimated glomerular filtration rate and hypertension ($p<0.001$).

Conclusion: The study demonstrates the diverse renal biopsy spectrum and reinforces the need for integrated clinicopathological interpretation using light microscopy, immunofluorescence and chronicity assessment.

Keywords: Renal biopsy, glomerulonephritis, focal segmental glomerulosclerosis, IgA nephropathy, lupus nephritis, histopathology.

INTRODUCTION

Medical kidney disease can present with many clinical syndromes, including nephrotic, nephritic and acute kidney injury, which can be caused by a number of different renal pathologies, and renal biopsy is a cornerstone investigation for medical kidney disease. The biopsy allows for a tissue diagnosis, activity and chronicity, as well as prognosis and therapeutic response [1-2].

The interpretation of modern kidney biopsy involves light microscopy, immunofluorescence and, if available, electron microscopy. This is a combination of approaches necessary to distinguish minimal change disease, focal segmental glomerulosclerosis, membranous nephropathy, IgA nephropathy, lupus nephritis, diabetic nephropathy and immune

complex-mediated glomerulonephritides [3]. The use of standardized classification schemes, like lupus nephritis and IgA nephropathy, has provided better reproducibility and outcome correlation [4, 5].

Variation in the spectrum of biopsy proven renal disease exists based on age, ethnicity, referral pattern, biopsy threshold, and availability of immunofluorescence and electron microscopy [6]. Renal biopsy, then, is useful in determining local disease burden and resource needs through retrospective biopsy audits. The present study was conducted on the objective of assessing the 5-year histopathological spectrum in native renal biopsies in a tertiary care centre and to correlate the major diagnoses with the clinical indications and chronicity features.

MATERIALS AND METHODS

Biopsies of the graft, renal mass biopsies, biopsies with fewer than 5 glomeruli, and those missing pertinent clinical details were excluded. Information pertaining to demographic data, indication for biopsy, serum creatinine, proteinuria, hematuria and appropriate serology was obtained from requisition forms and hospital records.

Biopsy cores were fixed in hematoxylin and eosin, periodic acid-Schiff, Masson trichrome and Jones methenamine silver stains for light microscopy. When fresh tissue was available, direct immunofluorescence was carried out for the determination of the presence of IgG, IgA, IgM, C3, C1q, kappa and lambda light chains. Diagnoses were made based on a combination of clinical information and light microscopy and immunofluorescence results. Glomerular sclerosis, interstitial fibrosis, tubular atrophy and vascular changes were used to assess chronicity by calculating the percentage of the glomeruli, interstitial area, tubular area and vascular area that were globally sclerosed.

Diseases were classified according to primary glomerular, secondary glomerular, tubulointerstitial, vascular or chronic sclerosing lesions. Data were analysed using SPSS version 26. Data were presented as mean +/-, or numbers and percentages, for continuous and categorical variables, respectively. Chronicity was compared with clinical parameters by using a chi-square test or independent t test, whichever was appropriate. A P value < 0.05 was deemed to be statistically significant.

RESULTS

A total of 312 adequate native renal biopsies were analyzed. The age ranged from 6 to 78 years, with a mean age of 34.9 +/- 16.8 years. Males constituted 171 cases and females 141 cases. Nephrotic syndrome was the most common indication, followed by nephritic syndrome and asymptomatic urinary abnormalities.

Primary glomerular diseases formed the largest category. Focal segmental glomerulosclerosis was the single most common diagnosis, followed by IgA nephropathy, membranous nephropathy and minimal change disease. Among secondary glomerular diseases, lupus nephritis predominated, especially among young adult females. Diabetic nephropathy and infection-related glomerulonephritis were also observed.

Immunofluorescence showed dominant IgA deposits in IgA nephropathy, granular IgG/C3 along capillary walls in membranous nephropathy and full-house staining in lupus nephritis. Interstitial fibrosis/tubular atrophy greater than 25% was seen in 82 cases and was significantly associated with hypertension, elevated serum creatinine and reduced estimated glomerular filtration rate.

Table 1. Clinical indications for renal biopsy

Indication	Number	Percentage
Nephrotic syndrome	133	42.6
Nephritic syndrome	59	18.9
Asymptomatic urinary abnormalities	44	14.1
Acute kidney injury	38	12.2
Systemic disease evaluation	38	12.2
Total	312	100.0

Systemic disease evaluation included suspected lupus nephritis, vasculitis and monoclonal gammopathy-associated renal disease.

Table 2. Major histopathological categories and diagnoses

Category/diagnosis	Number	Percentage
Primary glomerular diseases	198	63.5
Focal segmental glomerulosclerosis	60	19.2
IgA nephropathy	45	14.4
Membranous nephropathy	35	11.2
Minimal change disease	28	9.0

Other primary GN	30	9.6
Secondary glomerular diseases	72	23.1
Lupus nephritis	41	13.1
Diabetic nephropathy	18	5.8
Infection-related GN/others	13	4.2
Tubulointerstitial diseases	24	7.7
Vascular/chronic sclerosing lesions	18	5.8

GN = glomerulonephritis.

Table 3. Chronicity features and clinical association

Variable	IFTA <=25% (n=230)	IFTA >25% (n=82)	p-value
Age (years)	31.8 +/- 15.2	43.6 +/- 17.4	<0.001
Hypertension	74 (32.2%)	51 (62.2%)	<0.001
Serum creatinine (mg/dL)	1.4 +/- 0.8	3.1 +/- 1.7	<0.001
eGFR <60 mL/min/1.73m2	62 (27.0%)	55 (67.1%)	<0.001
Global glomerulosclerosis >25%	28 (12.2%)	46 (56.1%)	<0.001

IFTA = interstitial fibrosis/tubular atrophy; eGFR = estimated glomerular filtration rate.

DISCUSSION

It revealed that the most common indications for renal biopsy were nephrotic syndrome and that the major diagnosis category was primary glomerular diseases over the course of five years. This is similar to several tertiary centers in which biopsy series have been performed, in which proteinuric syndromes are the most important reason for renal biopsy [7].

The most frequent diagnosis in this group was focal segmental glomerulosclerosis. It could be a result of the actual disease burden, rising obesity and hypertension rates, and referrals for biopsy of steroid-resistant nephrotic syndrome [8]. The second most common primary glomerular disease was IgA nephropathy, which was often accompanied by hematuria and subnephrotic proteinuria. The scoring system developed by Oxford MEST-C scores has enhanced the prognostic evaluation of IgA nephropathy, and should be used when available [9].

Lupus nephritis was most common secondary glomerular disease, particularly in young women. The ISN/RPS classification permits a distinction between patterns of proliferation and membranous patterns, leading to immunosuppressive therapy [10]. Immunofluorescence can be useful in the diagnosis as a positive finding of full-house immunofluorescence (FHIF) should always be interpreted in combination with clinical and serological results.

Clinically significant were chronicity features. IFTA greater than 25% was also linked to hypertension, elevated creatinine and decreased eGFR, highlighting the significance of chronic tubulointerstitial damage as an important prognostic information irrespective of the primary diagnosis [11]. Chronicity grading can be standardized for better communication between the pathologist and the nephrologist [12].

There are limitations, such as retrospective design, selective availability of electron microscopy, and lack of long term renal outcome data. There may be cases under classified as some ultrastructural examination was not routinely available. The study, however, offers a valuable 5-year portrait of the course of biopsy-proven renal disease, and underscores the need for proper allocation of tissue for light microscopy and immunofluorescence [13-15].

The majority of cases presented as nephrotic syndrome emphasizes the importance of biopsy in the distinction of steroid responsive podocytopathies from immune complex and sclerosing glomerulopathies. Minimal change disease, focal segmental glomerulosclerosis and membranous nephropathy are all characterized by clinical proteinuria and therefore cannot be reliably differentiated, each of which has a different response to therapy and prognosis [1-3].

The size of the sample was a significant factor in the level of diagnostic confidence. Biopsies intact enough to have adequate cortex and glomeruli representative for the lesion were available for evaluation of focal lesions, segmental sclerosis, crescents and chronicity. Focal segmental glomerulosclerosis or lesions of vasculitis may be underdiagnosed if an inadequate sample is used because the characteristic lesion may only involve a minority of glomeruli [2]

Focal segmental glomerulosclerosis was the commonest diagnosis. This category includes primary and secondary and adaptive patterns, and it is best to evaluate histology in the context of the clinic, the level of proteinuria, the serum albumin, the body mass index and history of reduced nephron mass. Collapsing and tip lesions are specific and should be mentioned since they can have varying implications [8].

IgA nephropathy accounted for a significant percentage of biopsies and was often associated with hematuria. MEST-C scoring provides additional prognostic information over a diagnostic label alone. In retrospect, reporting mesangial hypercellularity, endocapillary proliferation, segmental sclerosis, tubular atrophy/interstitial fibrosis and crescents enhances communication between pathologists and nephrologists [5,6].

The most common secondary glomerular disease was lupus nephritis. It is important to classify into mesangial, proliferative, membranous and mixed patterns as activity and chronicity affect the intensity of immunosuppression. The diagnosis was confirmed by a full-house immunofluorescence pattern making additional confirmation by serological and clinical correlation necessary in atypical cases [4].

An important diagnosis for adult nephrotic syndrome was membranous nephropathy. While anti-PLA2R serology has altered the diagnostic algorithm, biopsy continues to provide information on stage, chronicity, secondary features and concurrent diabetic or vascular disease. So, serology and tissue evaluation must be considered complementary testing and not competing [3].

This is an important correlation between IFTA and renal failure, and highlights the importance of reporting chronicity. When active glomerular inflammation is treated, the degree of chronic tubulointerstitial injury may be used as a predictor of the limited reversibility. Clear categorization of fibrosis and tubular atrophy (T.A.) as percentages is useful in counseling patients on prognosis [11].

Lastly the audit identifies the logistical requirements for renal pathology services. Rashid et al. suggest that optimal interpretation of biopsy requires rapid triage of tissue, availability of immunofluorescence, trained technical personnel and close interaction between nephrologists and pathologists. It would be helpful to create a renal biopsy registry with standardized data fields so that future outcome studies and comparisons to other centers could be made [12-15].

The use of correlation of biopsy diagnosis with clinical syndrome is also given illustration. Minimal change disease tended to be associated with nephrotic syndrome, while IgA nephropathy tended to be associated with hematuria and with variable amounts of proteinuria. Such correlations support the diagnosis and can assist in the diagnosis of patients requiring repeat clinical review or additional stains.

The incidence of vascular lesions and hypertensive nephrosclerosis were less than that of the glomerular diseases but were clinically significant. When glomerular immune deposits are not present, chronic renal impairment might be due to arteriolar hyalinosis, intimal fibrosis and ischemic glomerular collapse. These changes shall be reported even if they are secondary findings.

The diagnostic group of tubulointerstitial diseases was smaller but these diseases are potentially reversible if they are diagnosed early. Drug history, infection, obstruction and systemic disease should be planned carefully in acute interstitial nephritis and acute tubular injury-chronic pyelonephritis pattern. In such instances, the lesion may be limited to the interstitium and very little may be seen in the glomeruli.

The final diagnosis was aided by immunofluorescence. Granular staining of the capillary walls was associated with membranous nephropathy, IgA staining of the mesangia was associated with IgA nephropathy, and full-house staining was associated with lupus nephritis. This means, however, that the absence of immunofluorescence tissue may lead to decreased diagnostic specificity, especially for immune complex disease [3,4].

In addition, electron microscopy was not available in all settings, which is typical of low-resource settings. The ultrastructural evaluation is very useful in thin basement membrane lesion, early membranous nephropathy, Alport syndrome, organized deposits and some podocytopathies. Electron microscopy may be used selectively, to maximize the resources and diagnostic yield.

The biopsy report should convert microscopic data into clinically meaningful categories to use in nephrology practice. Clinicians can estimate reversibility based on a diagnosis line, activity/chronicity comment, percentage of crescents, sclerosis degree, and IFTA and vascular changes to choose immunosuppression. Use of standardized templates helps to minimize omissions and standardize comparisons across time [11,12].

CONCLUSION

The most common native renal biopsy diagnoses were primary glomerular diseases, with the most predominant ones being focal segmental glomerulosclerosis, IgA nephropathy, membranous nephropathy and lupus nephritis. There was a strong association between chronic tubulointerstitial damage and renal function impairment. A clinicopathological integrated approach is still crucial for diagnosis and prognosis in renal disease.

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DECLARATIONS

Funding: None.

Conflict of Interest: The authors declare no conflict of interest.

Ethical Approval: The study was conducted in accordance with applicable ethical standards and approved by the appropriate ethics committee where required.

Informed Consent: Informed consent was obtained from all participants involved in the study where applicable.

Author Contributions: All authors contributed to the study conception, design, data collection, analysis, manuscript preparation, and approved the final version of the manuscript.

Data Availability: Data supporting the findings of this study are available from the corresponding author upon reasonable request.