

# **REPORTING AND INTERPRETING MEDICAL RENAL BIOPSIES – A REVIEW ARTICLE**

## **ABSTRACT**

Medical renal biopsy is an important tool in patient care in nephrology department. Systematic reporting of a renal biopsy eases the communication between the pathologist and the clinician, thereby improving patient care. H & E (Hematoxylin and eosin) sections alone cannot help to arrive at a diagnosis, Immunofluorescence, special stains and electron microscopy plays an important role too. To arrive at an accurate diagnosis, an expert renal pathologist, who has a thorough knowledge of renal pathology and as well as renal medicine is required to correlate tissue with clinical data. Although a lot of review articles regarding renal biopsies are published, review of literature covering all aspects of renal biopsy are a few especially from India.

*Keywords: H & E, Immunofluorescence, Electron microscopy*

## **INTRODUCTION**

For the accurate diagnosis of medical renal biopsies, renal biopsy is often essential. In addition, renal biopsy is frequently used to assess activity and chronicity, which is used to decide the appropriate therapy and determine prognosis [1]. A proper format is required to report renal biopsies so that all aspects are covered. Special stains supplement the light microscopy, especially Periodic acid–Schiff (PAS), Silver methenamine, Masson's trichrome and Congo red. It also helps to stain various components of the renal tissue [2]. Immunofluorescence (IF) is an irreplaceable technique which is used for accurate diagnosis in renal pathology, especially in diseases like IgA nephropathy (IgAN), C1q nephropathy (C1qN) and C3 glomerulopathy (C3G), which cannot be diagnosed without IF [3]. EM on the other hand must be done on all renal biopsies, but unfortunately, they are available only in huge centres [4].

## **COMMON INDICATIONS OF MEDICAL RENAL BIOPSY [5]**

Unexplained acute or rapidly progressive renal failure  
Nephrotic syndrome and significant non-nephrotic proteinuria  
Persistent glomerular haematuria  
Systemic diseases with renal involvement  
Staging lupus nephritis, classify IgA nephropathy, classify diabetic nephropathy  
Nephritic syndrome

## **ADEQUACY OF TISSUE SAMPLING**

An adequate renal biopsy is one that contains at least 10 glomeruli on light microscopy and should have at least one each for immunofluorescence and electron microscopy [6].

## **LIGHT MICROSCOPY (H & E SECTIONS & SPECIAL STAINS)**

H and E sections along with special stains is the back bone to report renal medical biopsies. H & E sections allow to count the number of glomeruli, general evaluation for percentage of cortex and medulla, cellular characteristics, type of inflammation and to locate the area of

interest i.e., whether the disease affects the glomerulus, interstitium, vessels or tubules. Special stains commonly used are PAS, Silver methenamine, Masson's trichrome and Congo red [7, 8]. The utility of the special stains is summarised in Table 1.

**Table 1: Utility of the special stains**

Special stains	Utility
PAS	Glomerular basement membrane, mesangium, tubular basement membrane, hyaline – pink to red
Silver methenamine	Basement membrane details – stains black
Masson's trichrome	Extracellular glomerular matrix and tubular basement membrane – blue or green
Congo red	Amyloid

### IMMUNOFLUORESCENCE

Fluorescein-labelled antibodies are used to examine immunoglobulins (IgG, IgM, and IgA), complement components (C3, C1q, and C4), fibrin, and kappa and lambda light chains. They may be also used for amyloid typing, collagen IV alpha chains in hereditary nephritis, IgG subclasses [8, 9].

### ELECTRON MICROSCOPY

Electron microscopy examines glomeruli ultrastructurally and aids to concentrate on deposits, very small deposits, fibrils and changes in cellular and basement membrane structure [4].

### INTERPRETATION OF RENAL BIOPSY

Low-power screening examination of the specimen helps in localizing that the defect is in glomerulus, tubules, and interstitium, or blood vessels [9].

- a) Distribution of lesion [10,11]

It is classified as:

- Diffuse: Changes occurring in all the glomeruli.
- Focal: Changes in few glomeruli only.
- Global: Whole glomerulus is involved.
- Segmental: Only some part of glomerulus is involved.

- b) Active Vs Chronic lesions [11,12]

The lesions need to be classified as either active or chronic. Table 2 summarises the examples of these lesions.

**Table 2: Examples of active and chronic lesions**

Active lesions	Chronic lesions
Necrosis	Fibrous crescents
Edema	Tubular atrophy
Cellular casts	Interstitial fibrosis
Active inflammation	Vascular sclerosis

- c) Abnormalities in glomerular capsule and glomerular basement membrane [12]

Table 3 summarises the common conditions and associated findings in relation to glomerular capsule while Table 4 elaborates in glomerular basement membrane.

**Table 3: Abnormalities in glomerular capsule**

	<b>Common conditions</b>	<b>Associated findings</b>
Capsular basement membrane thickening	Diabetes mellitus	Capsular drop
Capsular space obliteration	Glomerulonephritis Crescents or necrosis	

**Table 4: Abnormalities in glomerular basement membrane**

	<b>Common conditions</b>	<b>Associated findings</b>
1. Thick GBM		
a. Negative IF		
	Diabetic nephropathy	EM – Lamina densa thick No splitting by silver stain
	Hereditary nephritis	Silver stain irregular EM – Basket weaving
b. Positive IF		
	Membranous nephropathy	Spikes by silver stain Subepithelial deposits - EM
	Membranoproliferative glomerulonephritis	Silver stain – GBM splitting Subendothelial deposits - EM
	Amyloid	Positive light chains depending on type of amyloid
	Fibrillary glomerulonephritis	Variable splitting by silver Fibrils in EM
2. Thin GBM		
	Alport's syndrome	Silver stain irregular EM – Basket weaving
	Benign familial haematuria	Thin GBM - EM

GBM: Glomerular basement membrane, EM: Electron microscopy, IF: Immunofluorescence

d) Cellular proliferation [12, 13]

The three common locations of cellular proliferation are: Endothelial, epithelial, and mesangial cells. Abnormalities in these components with associated diseases in summarized in Table 5.

**Table 5: Abnormalities in glomerular components**

	<b>Common conditions</b>	<b>Associated findings</b>
1. Epithelial	Crescentic GN	
Linear GBM deposition	Anti-GBM disease	Positive anti-IgG linear staining along GBM
Immune complex	IgA nephropathy Post-infectious GN Lupus	Positive immune deposits in mesangium Positive immune deposits along capillary walls Full-house pattern of staining in mesangium and long capillary walls, tubuloreticular inclusions on EM

Pauci-immune	Granulomatosis with polyangiitis Microscopic angiitis	No deposits on IF No deposits on IF
2. Mesangial		
With nodule formation	Light chain deposition disease  Membranoproliferative GN  Diabetic nephropathy  Amyloidosis	Linear staining for light chains along GBM & TBM, granular deposits along GBM & TBM on EM Double contours with subendothelial deposits, cellular elements and new basement membrane formation PAS and silver positive nodules with negative IF Thick GBM & TBM PAS & silver negative nodules with positive IF staining for or light chains in AL amyloidosis
Without nodule formation	Post-infectious GN  Ig A nephropathy  C3 glomerulopathy	Positive granular IgG & C3 along capillary walls; Subepithelial humps and subendothelial deposits in EM IgA deposits in mesangium C3 in mesangium and along capillary walls on IF, and the absence of IgG
3. Endothelial	Post-infectious GN  Membranoproliferative GMN  SLE	Positive granular IgG & C3 along capillary walls; Subepithelial humps and subendothelial deposits in EM Positive granular IgG, IgM, C1q, C3 or light chains depending on cause, double contours on EM Full house staining on IF microscopy; mesangial, subepithelial, or subendothelial deposits depending on class of SLE

GN: Glomerulonephritis, TBM:Tubular basement membrane, SLE: Systemic lupus nephritis, GBM: Glomerular basement membrane.

e) Vascular abnormalities [14,15,16]

Vascular lesions are seen in afferent and efferent arterioles and respond to injuries. Moreover, due to the high blood flow in kidneys, they are more prone to vascular injury.

Table 6 shows the vascular lesions in renal biopsy.

**Table 6: Common vascular lesions in renal pathology**

	<b>Common conditions</b>	<b>Associated findings</b>
Sclerosis	Hypertension	Ischemic glomeruli with thickening of the glomerular basement membranes and wrinkling of the capillary loops
Thrombosis	HUS/TTP Malignant hypertension	Thrombi in glomerular capillaries, arterioles Onion skinning of the vessel walls with hypertrophy of the media
Fibrinoid necrosis	Malignant hypertension Polyarteritis nodosa HUS/TTP	Onion skinning of the vessel walls with hypertrophy of the media Arteritis, with fibrinoid necrosis and inflammation of vessel walls Thrombi in glomerular capillaries, arterioles
Vasculitis	Vasculitis	Depends on type. For e.g., in granulomatosis with polyangiitis, granulomatous inflammation
Emboli	Atheroembolism	Cholesterol atheroemboli in glomerular capillaries and arteries
Hyalinosis - Eccentric	Hypertension Diabetes	Ischemic glomeruli with thickening of the glomerular basement membranes and wrinkling of the capillary loops Diffuse and nodular glomerulosclerosis

HUS: Hemolytic uremic syndrome, TTP: Thrombotic thrombocytopenic purpura

f) Tubular abnormalities [15,16,17]

Tubular cells may exhibit acute reversible and irreversible damage (necrosis), intracellular accumulations, metabolic storage diseases and vacuoles. It may also show acute tubular necrosis and atrophy. Table 7 depicts the common tubular abnormalities.

**Table 7: Common tubular abnormalities**

<b>Lesions</b>	<b>Common conditions</b>	<b>Associated findings</b>
1. Necrosis	Ischemic and toxic ATN	Flattened tubular epithelial cells, mitotic figures
2. Edema	Ischemic and toxic ATN, thrombosis	Associated with interstitial inflammation; but no inflammation in renal vein thrombosis
3. Inflammation a. Polymorph b. Lymphocyte c. Eosinophil	Renal vein thrombosis  Acute interstitial nephritis, hypersensitivity reaction Churg- Strauss vasculitis	Increased neutrophils in glomerular capillaries Tubulitis Eosinophil infiltrate Eosinophil infiltrate
4. Granuloma a. Necrotising b. Confluent	Tuberculosis & fungal Sarcoidosis	Positive AFB stains in TB Perivascular granulomas
5. Intratubular material a. Pigmented cast	Myoglobin in rhabdomyolysis	Positive immunohistochemistry for myoglobin
6. Atrophy a. Focal b. Diffuse c. Disproportionate	Glomerular ischemia Advanced renal disease  Renal artery stenosis & renal vein thrombosis  Obstructive uropathy	Distended Bowman's space, with thickening and wrinkling of glomerular capillaries Focal global glomerulosclerosis  Tamm-Horsfall protein in tubules
7. Fibrosis a. Patchy	Chronic pyelonephritis	PAS-positive hyaline casts
8. Dilatation	Obstructive uropathy	Tamm-Horsfall protein in tubules

ATN: Acute tubular necrosis, AFB: Acid fast stain, TB: Tuberculosis

g) Interstitial abnormalities [18,19,20]

Interstitial has lesser number of abnormalities. The common ones are edema, inflammation, and fibrosis. Edema is considered acute while fibrosis chronic. Amyloid, immune complex deposits, and immunoglobulin light chains may also be seen in interstitium.

### **SIMPLE FORMAT FOR REPORTING MEDICAL RENAL BIOPSIES**

A simple format shown below may help a renal pathologist to report renal biopsies at ease without causing confusion to the nephrologist. This may also aid the pathologist to focus on important components also.

<b>Chart 1: Core of renal biopsy:</b>
<b>Glomerulus -</b> Number of glomeruli Globally sclerosed: Segmental sclerosis: Mesangial/ endothelial/ epithelial proliferation: Basement membrane/ capillary wall thickening: Wire loops: Inflammation:
<b>Tubules –</b> Edema: Inflammation: Atrophy: Casts: Amyloid:
<b>Interstitium –</b> Fibrosis: Edema: Inflammation: Amyloid:
<b>Vessels –</b> Hypertrophy: Hyaline or hyperplastic arteriosclerosis: Amyloid:
<b>Special stains –</b> PAS: Silver: Congo red: Masson Trichrome:
<b>Immunohistochemistry –</b> IgG: IgA: C3:
<b>Diagnosis:</b>

### **CONCLUSION**

Renal biopsy is a vital tool for understanding the pathology of various renal disease. It helps in evidence-based medicine and proper patient care. Both pathologists and nephrologists should work together for proper clinico-pathological correlation. H & E, special stains, IF, & EM together must be done routinely in all renal biopsies. If properly interpreted, renal biopsies are a great source for appropriate therapeutic strategy as well as to provide key prognostic information.

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