Original Article

# Gerontolizing Nephrology: Spectrum of Histopathological Findings of Kidney Biopsy in the Elderly

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## Abstract

**Introduction:** The spectrum of renal disorder in the elderly differs from the younger population. There is a paucity of literature regarding kidney biopsy in elderly. This study aims to highlight the clinical profile and histopathological spectrum of the elderly patient undergoing a renal biopsy. **Materials and Methods:** This retrospective study included all patients (age ≥60 years) undergoing native renal biopsies from January 2012 to December 2017. The clinical profile, laboratory parameters, and renal biopsy findings of these patients were recorded from the case files. **Results:** Out of 1656 renal biopsies performed during the study period, 230 (13.9%%) performed on the elderly were included. Mean age was 64.02 ± 7.87 years (Range: 60-87 years), and males were predominant (70.4%). The commonest indication for biopsy was nephrotic syndrome (NS) (49.6%) followed by Rapidly progressive renal failure (RPRF) (20.9%) and Acute Kidney Injury (AKI) (15.7%). The most frequent histological diagnosis was membranous nephropathy (15.2%) followed by amyloidosis (13.9%) and Focal Segmental Glomerulosclerosis (FSGS) (13.0%). The commonest cause of NS was MGN (29.8%) followed by FSGS (24.6%) and amyloidosis (22.8%). The commonest cause of nephritic syndrome was Diffuse Proliferative Glomerulonephritis (29.4%) and Membranoproliferative Glomerulonephritis (29.4%). Hypertensive nephrosclerosis (40.0%) and diabetic nephropathy (26.7%)) were the commonest histological diagnosis in the patients who underwent renal biopsy for clinical Chronic kidney disease. Crescentic GN (35.4%) and Myeloma cast nephropathy 14.6%) were the commonest cause of RPRF while Acute Tubular Necrosis (41.7%) was the commonest cause of AKI. None of the patients had major complications. **Conclusion:** Renal biopsy is safe in the elderly and provides a wealth of information with regards to the diagnosis and prognosis of renal disorder.

**Keywords:** *Elderly, India, nephrotic syndrome, renal biopsy*

## Introduction

At present, the elderly population has been increasing tremendously all over the world. As per the United Nations, the elderly population is growing faster than the total population practically all over the world.[1] India is also facing the same trend. The elderly population (≥60 years) increased from 7.6% in the year 2000 to 9.7% of the total population in the year 2015.[2] It is a well-known fact that, as age advances, there is a progressive loss of renal mass and function.[3]

The spectrum of renal disorder in the elderly differs from the younger population. Secondary renal diseases are considered more common, owing to the presence of various comorbidities such as diabetes and hypertension.[4] Glomerulonephritis as a primary diagnosis may be missed in the elderly because of systemic presentation. Similarly, multiple myeloma has been incidentally diagnosed after observing cast nephropathy in the kidney biopsy.[5] Overall, glomerulopathies can account for up to 25% of cases of renal diseases in the elderly.[6]

In general, there is reluctance among physicians in doing kidney biopsy in the elderly, because of the fear of complications. Age should not be considered as a barrier to kidney biopsy. It is considered to be a safe procedure even in the elderly and yields valuable information regarding diagnosis and prognosis.[7] As per recent data, kidney biopsy in the elderly has led to a modification in treatment in up to 40–70% of patients.[8-10]

There is a paucity of Indian literature regarding kidney biopsy in the elderly.



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The aim of our study was to describe the etiology, clinical presentation, and histopathological spectrum of elderly patients undergoing native renal biopsy at a tertiary care center in northwest India.

## Materials and Methods

All patients (age ≥60 years) undergoing native renal biopsies from January 2012 to December 2018 were included in this retrospective study conducted at our hospital. Patients with renal allograft biopsy, repeat renal biopsy, inadequate renal biopsy for interpretation, and inadequate medical records were excluded.

Renal biopsy was performed by a percutaneous technique with ultrasound guidance using an automated biopsy gun with a 16-gauge needle by a trained nephrologist. In most of the cases, two cores were obtained; one was fixed in formalin to be evaluated by light microscopy and the other by immunofluorescence studies. All the renal biopsies were examined by a pathologist. The electron microscopy facility was not available at our center.

All patients had a pre-biopsy evaluation, which included medical history and review of medical records, physical examination, and evaluation of bleeding and coagulation parameters. Hypertension was controlled in patients with hypertension prior to biopsy. All patients were kept under observation for 24 hours following renal biopsy. Complications of the renal biopsy were noted. Those with macroscopic hematuria were kept under observation until urine became clear. Severe complications were defined as severe renal bleeding requiring blood transfusions, acute kidney injury (AKI) from obstruction with blood clots, urosepsis, and death.

The clinical presentation, biochemical parameters and urine examination findings of the patients were obtained from case files. The main clinical syndromes requiring kidney biopsy were defined as follows:

1. Nephrotic syndrome was defined as proteinuria >3.5 g/day and hypoalbuminemia (<30 g/L) with clinical evidence of generalized edema
2. The nephritic syndrome was defined as patients having hypertension and edema along with hematuria, proteinuria, and dysmorphic red blood cells/red blood cell casts;
3. Rapidly progressive renal failure (RPRF), was defined as doubling of serum creatinine or a 50% decrease in glomerular filtration rate (GFR) over few weeks. Crescentic Glomerulonephritis (Crescentic GN) was defined as having >50% crescents in the biopsy
4. Chronic kidney disease (CKD) was defined according to the KDIGO 2012 guidelines
5. Acute kidney injury (AKI) was defined according to the KDIGO 2012 guidelines.

Statistical analysis was done in SPSS version 19.0. Percentages, mean and standard deviation were used to describe categorical and continuous variables, respectively.

## Results

During the study period, 1656 native renal biopsies were performed, of which 238 renal biopsies (14.4%) were performed on the elderly. Three (1.3%) biopsies were repeat renal biopsy and five (2.1%) biopsies were inadequate for interpretation and were not included in the analysis.

The mean age of the study population was 64.02 ± 7.87 years (range: 60–87 years). Males accounted for 70.4% ($n$ = 162) of the study population. Among the study population, 25 (10.9%) had diabetes, 134 (58.3%) had hypertension, and 32 (13.9%) had malignancy (multiple myeloma: 27, prostate cancer: 2, colon cancer: 1, lymphoma: 1 and lung cancer: 1).

Nephrotic syndrome was the commonest indication of renal biopsy ($n$ = 114, 49.6%) followed by RPRF ($n$ = 48, 20.9%), and AKI ($n$ = 36, 15.7%) [Table 1]. The commonest histological diagnosis was membranous nephropathy (MGN) ($n$ = 35, 15.2%) followed by amyloidosis ($n$ = 32, 13.9%), and focal segmental glomerulosclerosis (FSGS) ($n$ = 30, 13.0%) [Figure 1].

The most common histological finding in patients with nephrotic syndrome patients was MGN ($n$ = 34, 29.8%) followed by FSGS ($n$ = 28, 24.6%) and amyloidosis ($n$ = 26, 22.8%) [Figure 2a]. The commonest cause of nephritic syndrome was diffuse proliferative glomerulonephritis (DPGN) ($n$ = 5, 29.4%) and membranoproliferative glomerulonephritis (MPGN) ($n$ = 5, 29.4%) followed by IgA nephropathy ($n$ = 3, 17.6%) [Figure 2b]. Hypertensive nephrosclerosis ($n$ = 6, 40.0%), diabetic nephropathy ($n$ = 4, 26.7%), and amyloidosis ($n$ = 2, 13.3%) were the commonest histological diagnosis in the patients who underwent renal biopsy for CKD [Figure 2c]. Crescentic GN ($n$ = 17, 35.4%) and myeloma cast nephropathy, ($n$ = 7, 14.6%) were the commonest cause of RPRF, [Figure 2d] while acute tubular

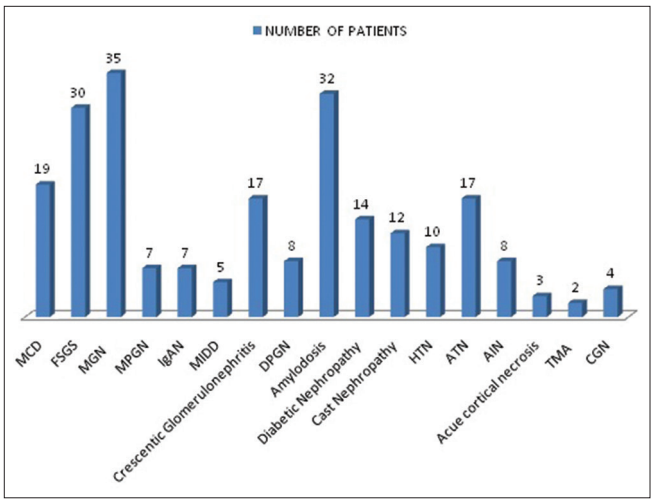


**Figure 1: Histopathological diagnosis in the study population**

**Table 1: Clinical syndrome and histological diagnosis in the elderly**

| Clinical syndrome | Nephrotic syndrome | Nephritic syndrome | Rapidly Progressive Renal Failure | Chronic Kidney Disease | Acute Kidney Injury | Total |
|---|---|---|---|---|---|---|
| **Histological diagnosis** | | | | | | |
| MCD | 18 | 0 | 1 | 0 | 0 | 19 |
| FSGS | 28 | 1 | 0 | 0 | 1 | 30 |
| MGN | 34 | 0 | 0 | 1 | 0 | 35 |
| MPGN | 1 | 5 | 1 | 0 | 0 | 7 |
| IgA Nephropathy | 1 | 3 | 2 | 1 | 0 | 7 |
| MIDD | 0 | 2 | 3 | 0 | 0 | 5 |
| Crescentic GN | 0 | 0 | 17 | 0 | 0 | 17 |
| DPGN | 0 | 5 | 3 | 0 | 0 | 8 |
| Amyloidosis | 26 | 0 | 1 | 2 | 3 | 32 |
| Diabetic Nephropathy | 6 | 0 | 4 | 4 | 0 | 14 |
| Cast Nephropathy | 0 | 0 | 7 | 0 | 5 | 12 |
| Hypertensive Nephrosclerosis | 0 | 0 | 3 | 6 | 1 | 10 |
| ATN | 0 | 0 | 2 | 0 | 15 | 17 |
| AIN | 0 | 0 | 1 | 0 | 7 | 8 |
| Acute Cortical Necrosis | 0 | 0 | 0 | 0 | 3 | 3 |
| TMA | 0 | 0 | 1 | 0 | 1 | 2 |
| CGN | 0 | 1 | 2 | 1 | 0 | 4 |
| TOTAL | 114 | 17 | 48 | 15 | 36 | 230 |

AIN: Acute interstitial nephritis, ATN: Acute tubular necrosis, CGN: Chronic glomerulonephritis, DPGN: Diffuse proliferative, FSGS: Focal segmental glomerulosclerosis, GN: Glomerulonephritis, MCD: Minimal change disease, MGN: Membranous nephropathy, MIDD: Monoclonal immunoglobulin deposition diseases, glomerulonephritis, MPGN: Membranoproliferative glomerulonephritis, TMA: Thrombotic microangiopathy

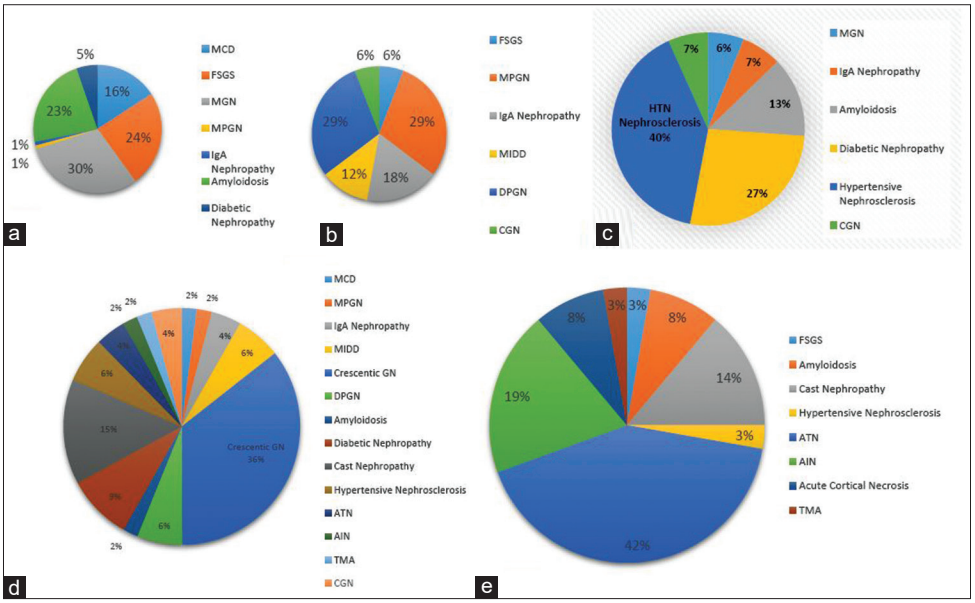


**Figure 2: (a) Renal biopsy findings in Nephrotic Syndrome. (b) Renal biopsy findings in Nephritic Syndrome. (c) Renal biopsy findings in Chronic Kidney Disease. (d) Renal biopsy findings in Rapidly Progressive Renal Failure. (e) Renal biopsy findings in Acute Kidney Injury**

necrosis (ATN) ($n$ = 15, 41.7%), and acute interstitial nephritis (AIN) ($n$ = 7, 19.4%) were the commonest cause of AKI [Figure 2e].

Among the primary glomerular diseases, three were positive for HBsAg (all three had MGN), two were infected with the hepatitis C virus (both had MGN), and one was infected with human immunodeficiency virus (HIV). Eight (42.1%) patients with MCD had exposure to nonsteroidal anti-inflammatory drugs (NSAID) prior to the onset of illness.

Five patients had solid organ malignancies. Three (prostate cancer: 2, colon cancer: 1) had MGN, one with lymphoma had crescentic GN, and the other with lung cancer had ATN. About 27 (11.7%) patients had multiple myeloma. Cast nephropathy was present in 12 (44.4%) patients; 5 (18.5%) patients had monoclonal

immunoglobulin deposition diseases (MIDD), 7 (25.9%) had primary amyloid while 3 (11.1%) had ATN. Four (14.8%) patients of multiple myeloma were retrospectively diagnosed, the initial clue being provided by renal biopsy.

Fourteen (56.0%) patients with diabetes had renal histology consistent with diabetic nephropathy while 11 (44.0%) had nondiabetic kidney disease, the most common being ATN ($n$ = 4) followed by MGN ($n$ = 3), FSGS ($n$ = 2), and IgA nephropathy ($n$ = 2). The majority of the patients with amyloidosis had secondary amyloidosis ($n$ = 25, 78.1%). The most common etiology being tuberculosis ($n$ = 16, 64%) followed by bronchiectasis ($n$ = 5, 25%) and others ($n$ = 4, 16%). Primary amyloidosis was diagnosed in seven (21.9%) patients who were diagnosed to have multiple myeloma.

Crescentic GN ($n$ = 17, 35.4%) was the most common cause of RPRF. Among crescentic GN patients, 7 were pANCA, 2 were cANCA, 2 were both cANCA and pANCA positive, 3 were ANCA negative, and 3 had the anti-GBM disease. The most common cause of ATN was sepsis ($n$ = 11, 64.7%) followed by drug ($n$ = 3, 17.6%). Four (50%) patients with AIN had a history of NSAID or antibiotic exposure before the onset of illness.

Only six patients had macroscopic hematuria following renal biopsy, all of which resolved with conservative treatment. No major complications were noted post-biopsy.

## Discussion

A kidney biopsy is considered the gold standard for establishing the diagnosis of renal parenchymal diseases.[11,12] There is a scarcity of Indian literature in terms of biopsy data in the elderly.[6,7] The possible reasons could be the perception of increased risk of complications in the elderly. Many glomerular diseases, as well as conditions like cast nephropathy, can be missed initially, given comorbid illnesses such as diabetes and hypertension which are common in the elderly. Previously, in view of the lack of data, glomerulonephritis was considered to be less common in the elderly, and they were not usually subjected to diagnostic or therapeutic interventions.[13] Over time, views have changed, and nowadays, even renal transplantation is performed easily in the elderly.[14] Thus biopsy in the elderly is necessary not only for diagnosis but also to guide appropriate therapeutic intervention.

Our study hopes to fulfill this lacuna and provide data regarding kidney diseases and indications of biopsy in the elderly [Table 1]. Almost 14% of the patients undergoing renal biopsy at our center were elderly. This is lower than the study from south India, which reported 30% elderly in their biopsy cohort[15] but is higher than that reported from north India[16,17] [Table 2]. This proportion of the elderly population is lower than those of developed countries like Europe and the USA, where it contributes to about 23% and 25% of kidney biopsies, respectively.[18,19] The reason could be a relative increase in the elderly population in the developed world and better healthcare access.

Males dominated our biopsy cohort making up to 70%, a finding noted by other Indian studies as well.[15-17] Nephrotic syndrome was the most common indication for elderly patients to undergo renal biopsy, a finding consistent with other Indian [Table 2] and western studies.[18,20] MGN was the commonest cause of nephrotic syndrome followed by amyloidosis. MGN has been reported as a common cause of nephrotic syndrome in most of the Indian literature [Table 2] and western studies.[21-23] A study conducted at our center has also reported MGN to be the most common cause of nephrotic syndrome in patients with age >40 years.[24] Amyloidosis was the second most common cause of nephrotic syndrome [Table 2]. It has also been quoted as the most common cause by a few studies.[17,25] The majority of these patients had secondary amyloidosis (78%), secondary to chronic diseases like tuberculosis and bronchiectasis. This is in contrast to the developed world where primary amyloidosis is more common. Secondary amyloidosis has also been found as a common cause of nephrotic syndrome from other Indian studies [Table 2].

The most common cause of nephritic syndrome was MPGN and DPGN. IgA nephropathy, a common cause of nephritic syndrome in young patients and the elderly Asian population of Japan and China,[25-27] was less common in our population.

RPRF was the second most common indication of renal biopsy. Crescentic GN, similar to other studies from northern India [Table 2] was the most common cause. In our study, pANCA positive pauci-immune crescentic GN was the most common cause of crescentic GN. However, studies from south India and east India[15,28,29] had found a low incidence of crescentic GN. This could be due to regional variations in the presentation of disease in the elderly. Cast nephropathy was the second most common cause of RPRF, similar to other Indian studies.[17] Hypertensive nephrosclerosis and diabetic nephropathy were the most common histological findings in patients undergoing biopsy for the diagnosis of chronic kidney disease. Forty-four percent of the diabetic patients had nondiabetic kidney disease, the commonest being ATN and membranous nephropathy, a diagnosis that has an implication on the management of these patients.

The elderly population is more prone to AKI because of anatomical changes, physiological decrease in GFR, and numerous factors such as exposure to contrast medium in angiography, nephrotoxic medications, atheroemboli, dehydration, and hypotension.[30] AKI was the third common indication for biopsy in our study, accounting for 13% of all biopsies performed, which is comparable

**Table 2: Comparison with other studies**

| Studies | Our Study | Koshy *et al.*[15] | Gupta *et al.*[17] | Bagchi *et al.*[16] | Kohli *et al.*[7] | Prakash *et al.*[6] |
|---|---|---|---|---|---|---|
| Patients (*n*) | 230 | 231 | 109 | 124 | 26 | 65(only glomerular diseases) |
| Duration of study | 2012–2017 | 2010–2016 | 2011–2014 | 2010–2014 | 200–2004 | 1998–2002 |
| Proportion of total biopsies done in the study period (%) | 13.8% | 33% | 8.7% | 7.2% | 12.4% | NA |
| Age (years) (mean±SD) | 64.02±7.87 | 64±6.03 | 67.7±6.4 | 64.9±4.9 | 63.5±3.2 | 64.2±0.83 |
| Age (years) cutoff | ≥60 years | ≥60 years | ≥60 years | ≥60 years | ≥60 years | ≥60 years |
| Common indications for biopsy | NS (49.6%)<br>RPRF (20.9%)<br>AKI (15.7%) | NS (30.4%)<br>Nephritic Syndrome (19.1%)<br>AKI (15.7%) | NS (37.4%)<br>RPRF<br>Nephritic syndrome | NS (39.5%)<br>AKI/ RPGN (32.3%) | AKI/ RPRF (73%)<br>NS (27%) | NS (61.5%)<br>Nephritic syndrome (29.2%)<br>RPGN (6.15%) |
| Most common histology in NS | MGN | MGN | Amyloidosis | MGN | MGN, Amyloidosis | MGN |
| Most common histology in RPRF/ AKI/Nephritic | RPRF-Crescentic GN<br>AKI-ATN<br>Nephritic-MPGN, DPGN | RPRF-PIGN<br>AKI- AIN<br>Nephritic-Benign Nephrosclerosis | RPRF-Pauci-immune crescentic GN,<br>Nephritic-MPGN | AKI/RPRF: Pauci-immune crescentic GN | NA | NA |
| Most common histology overall | MGN (15.2%)<br>Amyloidosis (13.9%)<br>AKI (13%) | Diabetic Nephropathy (14.3%)<br>CTIN (11.3%)<br>MGN (10.4%) | NA | MGN (22.6%)<br>FSGS (12.9%)<br>MCD (11.3%) | Crescentic GN, AIN | NA |

AKI: Acute kidney injury, AIN: Acute interstitial nephritis, ATN: Acute tubular necrosis, CGN: Chronic glomerulonephritis, CTIN: Chronic tubulointerstitial nephritis, DPGN: Diffuse proliferative, FSGS: Focal segmental glomerulosclerosis, GN: Glomerulonephritis, MCD: Minimal change disease, MGN: Membranous nephropathy, MIDD: Monoclonal immunoglobulin deposition diseases, glomerulonephritis, MPGN: Membranoproliferative glomerulonephritis, NS: Nephrotic syndrome, PIGN: Post-infectious glomerulonephritis, RPGN: Rapidly progressive glomerulonephritis, RPRF: Rapidly progressive renal failure, TMA: Thrombotic microangiopathy, NA: Data not available

to other Indian studies.[15,16] Sepsis, acute interstitial nephritis, and ATN due to NSAIDs were the common cause of AKI.

Kidney biopsy was pretty safe in our study, with only 2.6% of patients developing macroscopic hematuria. None of the patients developed any serious complication, highlighting the safety of renal biopsy in elderly patients as well.

Our study has few limitations. First, the retrospective design limits the amount of data that could be procured by medical records. Being a tertiary care center, most of the cases are referred primarily by physicians and might not depict the true profile of the renal disease in the elderly. Also, many patients refuse biopsy considering age and some are already on empirical immunosuppressive therapy prior to biopsy.

To conclude, renal biopsy is safe in the elderly and provides a wealth of information with regards to the diagnosis and prognosis of renal disorder.

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Nil.

### Conflicts of interest

There are no conflicts of interest.

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