***Original Article***

# *Patterns of biopsy-proved glomerular injury in Egyptian geriatric patients*

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## Abstract

**Background:** Chronic kidney disease (CKD) is considered a large burden in the elderly population. Many risk factors have been identified, however the pattern of involvement in this population remains unclear.
**Objectives:** To detect the pattern of glomerular injury in Egyptian geriatric population.
**Methods:** We performed a single-center, retrospective descriptive study on biopsy-proven renal diseases at Ain Shams University Pathology Unit; we included all biopsies with proved glomerular disease in geriatric patients aged ≥ 60 years (from 2018 to April 2023) to detect the pattern of glomerular injury in these patients throughout the last five years
**Results:** Ninety-six renal biopsies with proved glomerular injury were included. In our study the mean age was 66.938±5.068, also 27.08% of our population were diabetic while 56.25% were hypertensive. Mean values for serum creatinine and protein/creatinine ratio on presentation are 4.240±2.20 and 4.257±1.97 respectively. In our study the majority of biopsies showed Focal segmental Glomerulosclerosis (30.21%), it was followed by Membranous Glomerulonephritis (12.5%), Diabetic Glomerulosclerosis, Diffuse Proliferative Glomerulonephritis and Diffuse Glomerulosclerosis came next (11.46 ,11.46 and 10.42 % respectively)
**Conclusion:** Focal segmental glomerulosclerosis seemed to be the most prevalent type of glomerulonephritis in elderly Egyptian patients although these results need to verified on a larger scale of patients.
**Key Words:** Glomerulonephritis, elderly, geriatric

# Introduction

Geriatric patients are considered more at risk of renal dysfunction than younger population. Aging can contribute to renal dysfunction through several mechanisms including several changes that can be gross or at a cellular level, such as decline in physiological function and limited compensatory vascular reserve.
Renal biopsy in elderly doesn't have clear indications. Although many histopathological features can only be obtained by renal biopsy such as kidney injury severity, activity, and chronicity of lesions, also the presence of vascular changes. Despite this, the role of renal biopsy in elderly patients remains questionable by many physicians. Many authors support the role of renal biopsy in the aging society in reducing the risk of kidney disease progression by tailoring the treatment according to the specific pathological diagnosis, also some pathological diagnoses are frequently associated with underlying diseases like membranous glomerulonephritis with malignancy and AL amyloidosis with plasma cell dysplasia, this will in turn be a key factor in the treatment plan. (1). The main objective of this study was to assess the etiology and clinical presentations of renal disease in elderly Egyptian patients.

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**Materials and methods**

This was a single-center retrospective descriptive study that included 96 patients older than 60 years old with biopsy-proven glomerular lesions performed at Ain Shams University Hospitals from 2018 to 2023. Patients younger than that or with a predominant tubulointerstitial pathology were excluded. In all cases light microscopic (LM) evaluation and immunofluorescence (IFL) (for IgG, IgM, IgA, C3, C1q, kappa and lambda lights chains) were performed. Electron microscopy was also done in almost all cases to aid reaching a final diagnosis. The clinical categories of renal disease at the time of biopsy were defined as follows: nephrotic range proteinuria (≥3.5 g/day), nephritic presentation (oliguria, hematuria, azotemia) or a nephritic-nephrotic presentation.(2) For each group, we analyzed renal biopsy results, the clinical information available including patient's age, sex, initial serum creatinine (sCr) plus any available data such as viral markers (Hb s Ag, HCV Ab), C3, C4, urinary protein /creatinine ratio, serum protein electrophoresis and ANCA.
Ethical approval was obtained from Ain Shams University ethics committee

# Results

## Table (1) Clinical Characteristics of the study population

| | | | |
|---|---|---|---|
| **Age** | **Range** | 58-82 | |
| | **Mean ±SD** | 66.938±5.068 | |
| | | **N** | **%** |
| **DM*** | **No** | 70 | 72.92 |
| | **Yes** | 26 | 27.08 |
| **HTN**** | **No** | 42 | 43.75 |
| | **Yes** | 54 | 56.25 |
| **HCV***** | **No** | 88 | 91.67 |
| | **Yes** | 8 | 8.33 |
| **SLE****** | **No** | 92 | 95.83 |
| | **Yes** | 4 | 4.17 |
| **Others** | **No** | 95 | 98.96 |
| | **Renal Transplant** | 1 | 1.04 |
| **Clinical Presentation** | **Nephrotic Syndrome** | 20 | 20.83 |
| | **Nephritic Syndrome** | 20 | 20.83 |
| | **Nephritic-Nephrotic Presentation** | 56 | 58.33 |
| **Protein/Creatinine ratio** | **Range** | 0.4-10 | |
| | **Mean ±SD** | 4.257±1.971 | |
| **Creatinine on presentation** | **Range** | 0.6-10 | |
| | **Mean ±SD** | 4.240±2.202 | |
| | | **N** | **%** |
| **C3 and C4** | **Normal** | 82 | 85.42 |
| | **Low C3** | 6 | 6.25 |
| | **Low C4** | 2 | 2.08 |
| | **Low C3+C4** | 6 | 6.25 |
| **ANA** | **Negative** | 92 | 95.83 |
| | **Positive** | 4 | 4.17 |
| **ANCA** | **Negative** | 91 | 94.79 |
| | **Positive C** | 3 | 3.13 |
| | **Positive P** | 2 | 2.08 |

*Diabetes Mellitus
** Hypertension
*** Hepatitis C Virus
**** Systemic Lupus Erythematosus

## Table (2): Distribution of Glomerular pathology in the studied population

| **Biopsy** | | | |
|---|---|---|---|
| | | **N** | **%** |
| **FSGS*** | | 29 | 30.21 |
| **1ry or 2ry FSGS** | **1ry FSGS** | 9 | 31.03 |
| | **2ry FSGS** | 20 | 68.97 |
| **Membranous GN**** | | 12 | 12.50 |
| **Diabetic glomerulosclerosis** | | 11 | 11.46 |
| **Diffuse Glomerulosclerosis** | | 10 | 10.42 |
| **Ig A nephropathy** | | 3 | 3.13 |
| **MPGN***** | | 4 | 4.17 |
| **Type of MPGN** | **Type 1** | 4 | 100.00 |
| **Amyloidosis** | | 5 | 5.21 |
| **Type of amyloidosis** | **AL** | 3 | 60.00 |
| | **AA** | 2 | 40.00 |
| **Diffuse Proliferative GN** | | 11 | 11.46 |
| **Crescentic** | **No** | 3 | 27.27 |
| | **Yes** | 8 | 72.73 |
| **Type of Diffuse Proliferative** | **Post infectious** | 5 | 45.45 |
| | **Pauci-immune crescentic** | 6 | 54.55 |
| **Lupus Nephritis** | | 4 | 4.17 |
| **SLE class** | **Class 3** | 3 | 75.00 |
| | **Class 4** | 1 | 25.00 |
| **Podocytopathy** | | 2 | 2.08 |
| **Light chain disease** | | 1 | 1.04 |
| **Chronic allograft Nephropathy** | | 1 | 1.04 |
| **Minimal Change** | | 3 | 3.13 |

*Focal Segmental Glomerulosclerosis

** Glomerulonephritis

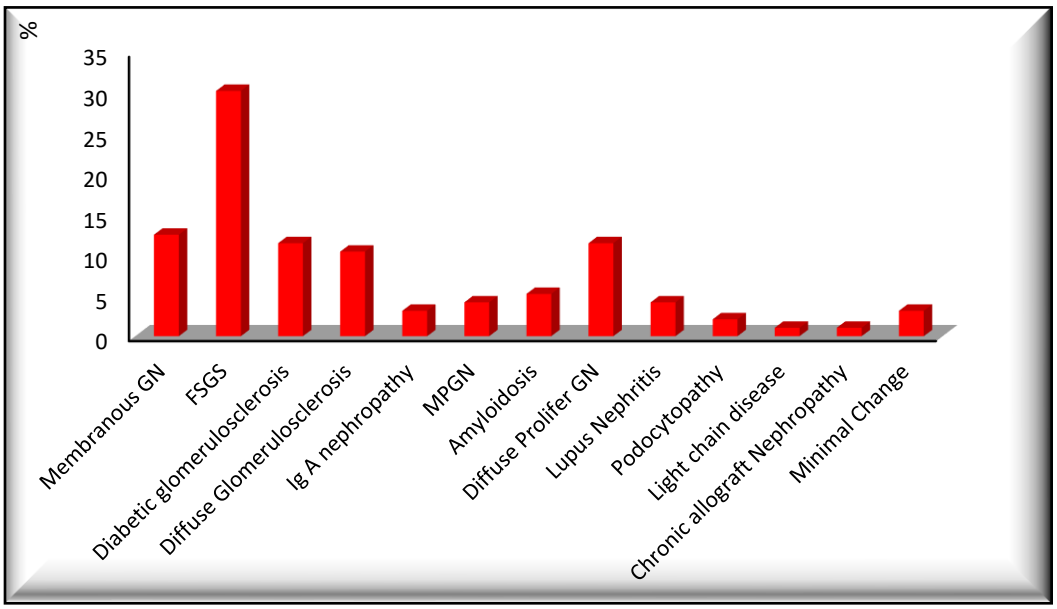


**Figure (1): Pathological Diagnoses of the study population**

**Table (3): Clinical and Pathological Diagnoses of the study population**

| | | | |
|---|---|---|---|
| **Age** | **Range** | 58-82 | |
| | **Mean ±SD** | 66.938±5.068 | |
| | | **N** | **%** |
| **DM** | **No** | 70 | 72.92 |
| | **Yes** | 26 | 27.08 |
| **HTN** | **No** | 42 | 43.75 |
| | **Yes** | 54 | 56.25 |
| **HCV** | **No** | 88 | 91.67 |
| | **Yes** | 8 | 8.33 |
| **SLE** | **No** | 92 | 95.83 |
| | **Yes** | 4 | 4.17 |
| **Others** | **No** | 95 | 98.96 |
| | **Renal Transplant** | 1 | 1.04 |
| **Clinical Presentation** | **Nephrotic Syndrome** | 20 | 20.83 |
| | **Nephritic Syndrome** | 20 | 20.83 |
| | **Nephritic-Nephrotic Presentation** | 56 | 58.33 |
| **Protein/Creatinine ratio** | **Range** | 0.4-10 | |
| | **Mean ±SD** | 4.257±1.971 | |
| **Creatinine on presentation** | **Range** | 0.6-10 | |
| | **Mean ±SD** | 4.240±2.202 | |
| | | **N** | **%** |
| **C3 and C4** | **Normal** | 82 | 85.42 |
| | **Low C3** | 6 | 6.25 |

| | | | |
|---|---|---|---|
| | **Low C4** | 2 | 2.08 |
| | **Low C3+C4** | 6 | 6.25 |
| **ANA** | **Negative** | 92 | 95.83 |
| | **Positive** | 4 | 4.17 |
| **ANCA** | **Negative** | 91 | 94.79 |
| | **Positive C** | 3 | 3.13 |
| | **Positive P** | 2 | 2.08 |
| **Biopsy** | **Membranous Nephropathy (MN)** | 12 | 12.50 |
| | **Focal Segmental Glomerulosclerosis (FSGS)** | 29 | 30.21 |
| | **1ry FSGS** | 9 | 31.03 |
| | **2ry FSGS** | 20 | 68.97 |
| | **Diabetic glomerulosclerosis** | 11 | 11.46 |
| | **Diffuse Glomerulosclerosis** | 10 | 10.42 |
| | **Ig A nephropathy** | 3 | 3.13 |
| | **Membranoproliferative Glomerulonephritis (MPGN)** | 4 | 4.17 |
| | **Type 1** | 4 | 100.00 |
| | **Amyloidosis** | 5 | 5.21 |
| | **AL** | 3 | 60.00 |
| | **AA** | 2 | 40.00 |
| | **Diffuse Proliferative GN** | 11 | 11.46 |
| | **Post infectious** | 5 | 45.45 |
| | **Pauci-immune crescentic** | 6 | 54.55 |
| | **Crescentic GN** | | |
| | **Yes** | 8 | 72.73 |
| | **No** | 3 | 27.27 |
| | **Lupus Nephritis** | 4 | 4.17 |
| | **Class 3** | 3 | 75.00 |
| | **Class 4** | 1 | 25.00 |
| | **Podocytopathy** | 2 | 2.08 |
| | **Light chain disease** | 1 | 1.04 |
| | **Chronic allograft Nephropathy** | 1 | 1.04 |
| | **Minimal Change GN** | 3 | 3.13 |

## Discussion

Elderly patients compromise a large group among patients with chronic kidney disease (CKD). The elderly is liable to kidney diseases but with a different clinical morphological picture which may be attributed to aging. Senescence can be associated with a decline in eGFR by 0.8–1.7 ml/min per year, thus limiting the renal reserve and making the elderly more liable to other risk factors, common in the geriatric population,

such as hypertension, diabetes, cardiovascular disease and nephrotoxic drugs or contrast media (3). The complex background as well as different clinical and morphological presentation may counteract disease recognition, hindering accurate diagnosis and proper treatment. In many situations renal biopsy is greatly required for accurate diagnosis. Unfortunately, the older the age, the less percentage of patients are precisely diagnosed and most of the patients older than 55 years are labelled as 'CKD of unidentified origin' (4).

In our study the mean age was 66.938±5.068, also 27.08% of our population were diabetic patients while 56.25% were hypertensive patients. Only 4 patients had history of systemic lupus erythematosus while 8 patients had hepatitis C, however none of them had been treated prior to the renal biopsy. Only one patient had received a renal transplant 5 years prior from a living nonrelated donor.

20% of the patients had nephrotic syndrome, the same percentage also had a nephritic presentation while the majority of the patients 58.33% had a nephritic-nephrotic presentation. Mean values for serum creatinine and protein/creatinine ratio on presentation are 4.240±2.20 and 4.257±1.97 respectively. Complement levels were normal in the majority of patients 85.42; c3 was consumed in 6.25% of the patients while c4 was consumed in only 2.08% of the cases.

In our study the majority of biopsies showed Focal segmental Glomerulosclerosis (30.21%), it was followed by Membranous Glomerulonephritis (12.5%), Diabetic Glomerulosclerosis, Diffuse Proliferative Glomerulonephritis and Diffuse Glomerulosclerosis came next (11.46 ,11.46 and 10.42 % respectively).

Other diagnoses included Amyloidosis (5.21%), MPGN (4%), Lupus Nephritis (4.17%), Minimal Change Glomerulonephritis (3%), Podocytopathy (2.08%), Light Chain disease and Chronic Allograft Nephropathy (1.04%,1.04%).

FSGS was found to be secondary in most of the cases (68.97%) and primary in only 31.03% of the cases. Although 26 patients had history of diabetes mellitus only 11 patients had diabetic glomerulosclerosis while the rest had alternative diagnoses.

Perkowska-Ptasinska et al. recruited patients from 14 different centers in Poland and they established that nephrotic syndrome (55.6%) was more predominant in the elderly in contrast to the younger patients where non-nephrotic proteinuria dominated (52.5%) .In elderly patients the major histological types were MGN (25%), amyloidosis (20.2%) and FSGS (20.2%) while FSGS (17.5%), MGN (16.9%) and IgAN (16.8%) predominated in the young cohort.

Among elderly patients, hematuria was frequently seen with amyloidosis (25.2%) (5).

In the previous study membranous GN was the most prevalent lesion, while in our study FSGS came at first place, however in both settings the majority of the cases had morphological and clinical features suggestive of secondary FSGS. The etiology was clearly unidentified although in elderly patients secondary FSGS may be attributed to many factors such as aging, hypertension and arteriosclerosis.

Another similar study that was based in India and recruited 132 patients with male predominance. The predominating lesion was focal segmental glomerulosclerosis (FSGS) ;66.6% of patients involved had high serum creatinine values. (6).

In another study based also in India and including 347 native kidney biopsies where only 50 patients were elderly (14.40%) with a mean age of 66.34 ± 5.24 years. Males predominated the study population (70%). The most common clinical presentations were nephrotic syndrome (36%) and acute kidney injury (24%). The most common lesions were membranous nephropathy (MN) (14%) and focal segmental glomerulosclerosis (12%). Diabetic nephropathy predominated in older patients (63.6%) while lupus nephritis was found more in young adults (35.8%) (7)

Another study by Prakash et al. included 315) elderly Indian patients aged from 60 to 90 years and evaluated for the presence of glomerular diseases in the period between 1998 and 2002. Glomerular lesions were found in 20.6% of the cases (65 patients). The mean age of the patients was 64.17 +/- 3.83) years. The clinical presentation was divided as follows: nephrotic syndrome in 40 patients (61.5%), acute nephritic syndrome in 19 patients (29.2%), rapidly progressive GN in 4 patients (6.15%) and asymptomatic urinary abnormality in 2 patients (3.0%). Primary glomerular diseases were seen in 47 patients (72.3%) while secondary lesions were seen in 18 patients (27.6. Idiopathic membranous nephropathy predominated as the most frequent cause for nephrotic syndrome in 11patients (27.5%). Diabetic Nephropathy was found next 9 patients (22.5%). Amyloidosis was found in 6 patients (15%. Post infectious GN etiology was the most common cause of acute GN (82.6%). Crescents were present in 4 patients (17.4%) patients. Unlike western countries, cases of Pauci-immune crescentic GN were not observed. Asymptomatic urinary abnormalities were found in association with Mesangiocapillary GN and mesangioproliferative in two patients only (8).

Another study that took place in Jordan at the University hospital from

2007 to 2018 and included pathological reports of all patients of all ages with native renal biopsies. Diabetic Nephropathy proved to be the most common GN in the elderly (9).

Another study performed on 500 renal specimens of American patients (449 patients and 51 cadavers) with ages between 60 and 89 years from the registry of AFIP (Armed Forces Institute of Pathology). The clinical presentations ranged from hypertension, proteinuria to full blown nephrotic or nephritic syndrome and renal failure. The most common diagnoses were Minimal change disease (60 patients, 12%), followed by focal proliferating glomerulonephritis (59 patients, 11.8%) and lastly membranous glomerulonephritis (51patients, 10.2%) (10).

Labeeuw et al. performed a similar study in France, however they included 177 patients aged more than 75 years and found that the most common histological types found were: Membranous nephropathy (MN), IgA Nephropathy (IgAN) and minimal change disease (MCD) . Nephrotic syndrome constituted about 51% of renal biopsies included and the histological diagnoses were: Membranous Glomerulonephritis (36%), MCD (33%) and amyloidosis (12%); Another clinical presentation was chronic renal failure which constituted 25% of the patients and the histological diagnoses were: Chronic interstitial nephritis (17%) followed by benign nephrosclerosis (12%) and lastly IgAN (12%).Acute or rapidly progressive renal failure constituted 18% of the patients and the histological diagnoses were : Acute tubular necrosis (36%) followed by Crescentic GN (16%) and lastly IgAN (12%). Isolated proteinuria was frequently associated with IgAN. The authors support greatly the role of biopsy in older patients (11).

Verde et al. analyzed data from the Spanish registry where 71 patients (0.4% out of 17,680 renal biopsies provided by the registry) were from patients older than 85 years. Acute kidney injury (AKI) (47%) and nephrotic syndrome (32%) were the most common clinical presentations. Amyloidosis was established as the most frequent diagnosis (16.9%), then pauci-immune crescentic glomerulonephritis mostly due to systemic vasculitis (14.1%) came in the second place. Upon correlating the histological data with clinical presentation, amyloidosis was frequently associated with both AKI (18.8%), and nephrotic syndrome. Crescentic glomerulonephritis was related to different clinical presentations such as chronic kidney disease and AKI(40%) . The authors advocated the role renal biopsy in the very elderly stating that it can provide useful information (12).

Soares et al. included patients presented with nephrotic syndrome in Brazil who are older than 65 years and were biopsied from 2012 to 2019. Out of 123 included renal biopsies 44 (35.8%) were due to nephrotic syndrome; where the main diagnoses were found to be membranous nephropathy (29.5%), amyloidosis (22.7%), then focal segmental glomerulosclerosis (FSGS) which was divided equally into non collapsing FSGS (9.1%) and collapsing FSGS (9.1%). Minimal change disease (MCD) was the least type with interstitial fibrosis and acute tubular necrosis (ATN) was found to be the least in amyloidosis (13).

Several studies investigated the pattern of Biopsy-proved glomerular injury in Egypt. However, only few included geriatric populations.

Afifi et al. studied the pattern of renal diseases among elderly Egyptians patients in a multi-centric study based in the hospitals of both Ain Shams University and Nasser Institute, however from 220 patients renal biopsy was performed in only 20 patients. The histological diagnoses were Focal necrotizing GN (20%) followed by Membranous nephropathy (50%) and lastly renal amyloidosis (30%). Chronic Tubulointerstitial nephritis was associated with NSAIDs intake. (14).

As we can see so far from the literature the pattern of glomerular injury in elderly seems to be diverse and variable according to the ethnicity of the involved population. As regards the Egyptian population, this topic needs to be explored further, however this seems limited to a certain extent by the limited number of available biopsies that may be related to the multiple co-morbidities and frailty of this population.

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