

## Histopathological findings in elderly patients

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### ABSTRACT

**Introduction:** The elderly population has significantly increased worldwide and recent studies have evidenced a 10-year increase in Brazilian life expectancy. Similarly to other comorbidities, glomerular diseases are also observed in the elderly, and, in that age group, kidney biopsy emerges as a fundamental diagnostic tool to help disease management, preventing unnecessary therapies. **Objective:** To establish the frequency of histological diagnoses in the elderly undergoing kidney biopsy, with an emphasis on glomerulopathies (GPs), at two Brazilian universities.

**Methods:** Retrospective assessment of kidney biopsy reports of the Department of Pathology of UNIFESP (patients aged 60 years or above, from 01/01/1996 to 12/31/2003) and of the outpatient clinic of GPs of NIEPEN. The studies of transplanted kidneys and nephrectomies were excluded. The following data were analyzed: age; sex; clinical syndrome at presentation; and histological diagnosis (light microscopy and immunofluorescence). Nephropathies were classified as primary GPs, secondary kidney diseases, nonglomerular diseases, and others. **Results:** One hundred and thirteen biopsies were assessed, the mean age of patients was  $66.0 \pm 6.0$  years, and the male sex prevailed (54.8%). The most common clinical presentation was nephrotic syndrome (32.7%), followed by acute and chronic kidney failure (18.6%, each). Glomerular diseases were as follows: membranous nephropathy (MN), 15%; hypertensive nephrosclerosis, 11.5%; focal segmental glomerulosclerosis and vasculitis/crescentic GN, 9.7% each; amyloidosis, chronic glomerulonephritis, and minimal change disease, 7.1% each; diffuse proliferative

GN, 4.4%; IgA nephropathy and lupus nephritis, 2.7% each. Primary GPs predominated (45.2%) as compared with other nephropathies. **Conclusion:** Nephrotic syndrome was the major indication for kidney biopsy. Regarding the kidney histological diagnoses, glomerular diseases predominated, in particular MN and hypertensive nephrosclerosis, findings compatible with previous studies in the area, but rarely assessed among us. It is clear that the diversity of diagnoses and differentiated treatments justify kidney biopsy for decision making in that group of patients.

**Keywords:** aged, biopsy, glomerulonephritis, nephrotic syndrome, chronic kidney failure.

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### INTRODUCTION

In general, the elderly population has significantly increased. This results from technological innovation and advances in quality of life, as well as from the decline in the fecundity and mortality rates in each year. These factors contribute to the aging profile our country has shown lately.<sup>1</sup>

According to the Brazilian Institute of Geography and Statistics (IBGE), the aging index indicates changes in the Brazilian population longevity. According to the 2008 demographic census, for every 100 children aged 0 to 14 years, there were 24.7 elderly aged 65 years or above,

and the projection for 2050 is an increase to 172.7 elderly.<sup>1</sup> Another evidence of the population aging is the increase in life expectancy of Brazilians, currently of 72.78 years. That mean should continue to increase and, by 2050, life expectancy is expected to have increased to 81.29 years, equaling that of countries with high human development index, such as Iceland (81.8 years) and Japan (82.6).<sup>1</sup>

The use of new instruments and technology appears as a perspective for approaching that age group. Thus, it is increasingly clear that advanced age by itself is no longer an obstacle to medical investigations or interventions, considering that invasive diagnostic procedures and even therapeutic tools have become safer. Nephrology reflects that reality in the increasing number of elderly patients undergoing renal replacement therapies and in the higher demand for kidney transplantation.<sup>2</sup>

Regarding glomerular disease, the histopathological assessment of renal tissue is the investigation method capable of establishing the definitive diagnosis. In addition, the information obtained by use of kidney biopsies does not only identify the specific diagnosis, but also provides a prognostic index, helping in deciding the therapeutic management in each case.<sup>3,4</sup>

The incidence of glomerulopathies in the elderly has greatly varied in the different series analyzed, from almost null to up to 25%.<sup>5</sup> The diagnosis of glomerular disease may be underestimated in the elderly, because its symptoms can be attributed to asymptomatic systemic diseases and urinary abnormalities can be diagnosed as urinary tract diseases, such as prostatitis. In addition, in the presence of comorbidities, many professionals still maintain a conservative attitude towards invasive diagnostic procedures and therapeutic interventions in that population, because of the risk of complications.<sup>6</sup>

Considering that the procedure is safe and that glomerular diseases, even in that age group, can be treated, or, on the contrary, that unnecessary immunosuppression can be prevented, kidney biopsy appears as an unquestionable diagnostic tool for the elderly.<sup>7,8</sup>

This study aimed at assessing the most frequent clinical presentation and histopathological diagnoses in the elderly population suspected of having glomerular disease at the Federal University of São Paulo/ Paulista Medical School (UNIFESP/EPM) and outpatient clinic of glomerulopathies of the Interdisciplinary Nucleus of Education and Research in Nephrology (NIEPEN) of the University of Juiz de Fora, in the state of Minas Gerais.

## METHODS

A retrospective analysis was conducted with 92 kidney biopsy reports from elderly patients of the Department of Pathology of UNIFESP, from 01/01/1996 to 12/31/2003, and with 21 kidney biopsy reports from the outpatient clinic of glomerulopathies of NIEPEN, from 01/01/1996 to 12/31/2009.

Individuals aged 60 years or above were arbitrarily considered elderly. For each case, the following data were extracted from the biopsy reports and analyzed: age; sex; clinical syndrome at presentation; and histological diagnosis. Biopsies from transplanted kidneys and nephrectomies were not included in the study.

According to the description in the requisition form for kidney biopsy completed by the assistant nephrologist, the clinical syndromes at presentation were divided as follows: nephrotic syndrome; nephritic syndrome; urinary abnormalities; acute kidney failure (AKF); and chronic kidney failure.

Histological diagnosis was established by use of light microscopy and immunofluorescence. The nephropathies were classified as follows: primary glomerulopathies; secondary kidney diseases; nonglomerular diseases; and others. Primary glomerulopathies referred to conditions in which the kidneys were the only organs affected, while in secondary kidney diseases, there was evidence of associated systemic disease.

## RESULTS

One hundred and thirteen kidney biopsies of patients aged 60 years or above were assessed. Their mean age was  $66.0 \pm 6.0$  years. The male sex prevailed (54.8%). The primary glomerulopathies were the most frequent, accounting for 45.2% of the kidney biopsies, followed by secondary kidney diseases, accounting for 35.4% of the sample. Table 1 shows the classification of the glomerulopathies and their frequencies.

Nephrotic syndrome was the most common clinical presentation, indicating kidney biopsy in 32.7% of the cases. Acute and chronic kidney failure accounted for kidney biopsy indication in 18.6% of the patients. Asymptomatic urinary abnormalities affected 16.8% of the elderly at presentation. In 10.6% of the biopsy reports, there was no description of the syndrome responsible for kidney biopsy indication (Table 2).

Figures 1 and 2 show the most frequent diagnoses in cases of nephrotic syndrome and acute kidney failure, with predominance of membranous nephropathy and vasculitis, respectively.

The most common histopathological findings in the elderly are shown in Table 3. Membranous

nephropathy was the most frequent disease, observed in 15% of kidney biopsies. Hypertensive nephrosclerosis was the second most common finding in the elderly, totaling 11.5% of all biopsies. Vasculitis and focal segmental glomerulosclerosis (FSGS) were equally frequent and identified in 9.7% of the cases. Amyloidosis, minimal change disease, and chronic glomerulonephritis accounted for 7.1% of the glomerular diseases in the elderly.

Immunofluorescence findings were positive in 30% of the cases and negative in 36%. In the remaining biopsies (34%), the specimen was insufficient for analysis (Figure 3).

Of the primary glomerulopathies, membranous nephropathy was the most common, followed by FSGS and minimal change disease, accounting for 33.3%, 21.6%, and 15.7% of the cases, respectively (Figure 4).

Figure 5 shows the most frequent secondary diseases. The major cause of secondary kidney disease in the elderly was hypertensive nephrosclerosis (32.5%), followed by vasculitis and amyloidosis, accounting for 27.5% and 20.0%, respectively. Only three cases of lupus nephritis were observed.

## DISCUSSION

Despite the limitations of the retrospective approach, this study has epidemiological importance in face of the scarcity of similar studies, mainly in Brazil. Through review of kidney biopsy reports from two Brazilian regions, the spectrum of glomerular diseases was assessed, as were the major indications for kidney biopsy in the population over the age of 60 years.

In our study population, the male sex predominated slightly, in accordance with other studies assessing populations of the same age.<sup>9,10,11</sup> On the other hand, assessments of patients over the age of 80 years found a higher frequency of women, possibly because of their longer life expectancy.<sup>12,13</sup>

Similarly to that found in the younger population, nephrotic syndrome is a very common and unquestionable condition requiring kidney biopsy.<sup>14</sup> In our study, nephrotic syndrome was the major indication for kidney biopsy, followed by acute kidney failure, a finding consistent with those of other studies with the same age bracket.<sup>15,16,10,11,17</sup> In a recent publication, the Spanish Registry of Glomerulonephritis has also found a similar profile, but with an even higher percentage of AKF than the one here reported. Despite the unfavorable evidence against kidney biopsy in AKF in the elderly, because of the high clinical-pathological

correlation,<sup>18,19</sup> Haas has reported that, in one third of the elderly, the histopathological diagnosis differed from clinical suspicion.<sup>15</sup> In our study, the major

**Table 1** DEMOGRAPHIC AND HISTOLOGICAL DATA

Age (years)	66 ± 6
Sex (%)	
Female	45.1
Male	54.8
Histological classification (%)	
Primary glomerulopathies	45.2
Secondary glomerulopathies	35.4
Nonglomerular kidney diseases	9.7
Others	9.7

**Table 2** DISTRIBUTION OF THE CLINICAL SYNDROMES

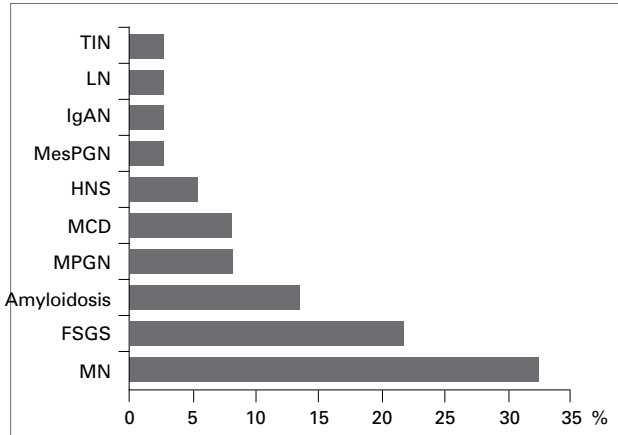
Nephrotic syndrome	32.7
Acute kidney failure	18.6
Chronic kidney failure	18.6
Asymptomatic urinary abnormalities	16.8
Ignored	10.6
Nephritic syndrome	2.6

cause of AKF was vasculitis (31.8% of AKF causes), followed by “acute diffuse glomerulonephritis” and acute tubular necrosis (ATN), both with 18.2% of the AKF causes. Moutzouris *et al.*,<sup>13</sup> assessing a population over the age of 80 years with AKF, reported ATN in only 5% of the cases, evidencing excellent clinical screening for kidney biopsy by the assistant nephrologist.

Membranous nephropathy is known to be the most common histological pattern in the elderly, and its frequency varies depending on the population studied and the indications for biopsy of each service.<sup>2,6,7,9,20,21</sup> In our study, membranous nephropathy was also the most frequent glomerular disease, corresponding to 15% of the sample, a finding similar to that of a recent survey of the Paulista Registry of Glomerulopathies, whose percentage was 13.1%.<sup>22</sup>

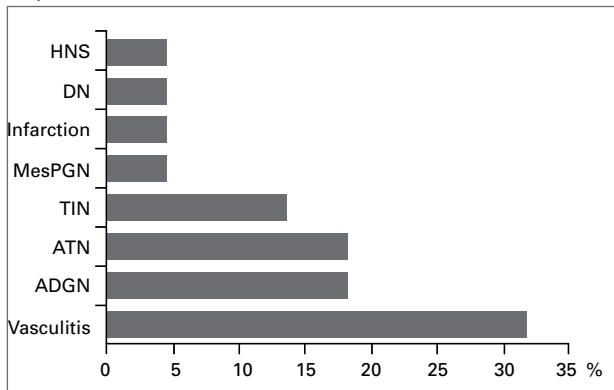
In our study, hypertensive nephrosclerosis was the second most common histological pattern, a finding justified by the high prevalence of arterial hypertension in that age group, which can reach up to 50%.<sup>23</sup> However, hypertensive nephrosclerosis can be a

**Figure 1.** Frequency of glomerulopathies in nephrotic syndrome.



MN: Membranous nephropathy; FSGS: focal segmental glomerulosclerosis; MPGN: membranoproliferative glomerulonephritis; MCD: Minimal change disease; HNS: Hypertensive nephrosclerosis; MesPGN: mesangioproliferative glomerulonephritis; IgAN: IgA nephropathy; LN: lupus nephritis; TIN: tubulointerstitial nephritis

**Figure 2.** Frequency of glomerulopathies in acute kidney failure.



HNS: Hypertensive nephrosclerosis; DN: Diabetic nephropathy; MesPGN: mesangioproliferative glomerulonephritis; TIN: tubulointerstitial nephritis; ATN: acute tubular necrosis; ADGN: acute diffuse glomerulonephritis.

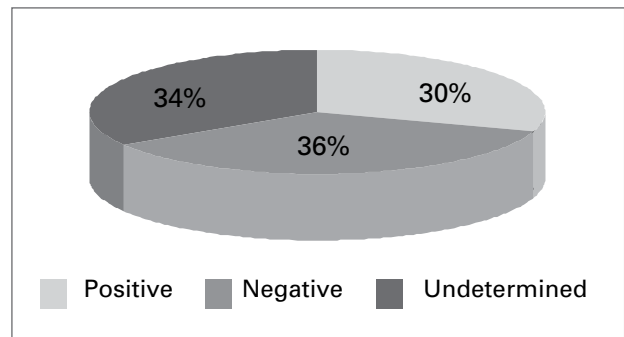
**Table 3**

DISTRIBUTION OF LIGHT MICROSCOPY FINDINGS

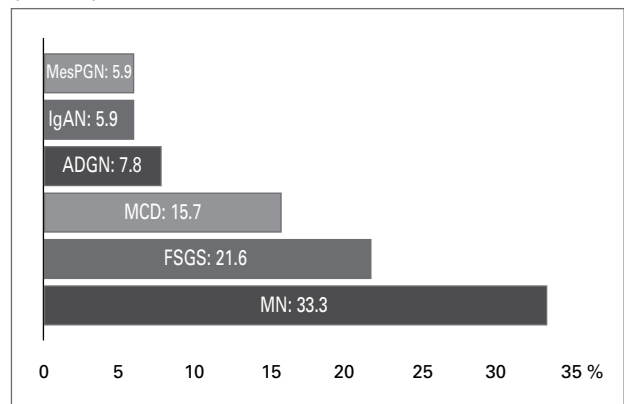
Histopathological diagnoses	n	%
Membranous nephropathy	17	15
Hypertensive nephrosclerosis	13	11.5
Focal segmental glomerulosclerosis	11	9.7
Vasculitis	11	9.7
Amyloidosis	08	7.1
Chronic glomerulonephritis	08	7.1
Minimal change disease	08	7.1
Acute diffuse glomerulonephritis	05	4.4
IgA nephropathy	03	2.7
Lupus nephritis	03	2.7
Others	26	23
<b>Total</b>	<b>113</b>	<b>100</b>

difficult diagnosis, since nephrosclerosis is a histological lesion also observed in patients with ischemic nephropathy secondary to vascular kidney disease.<sup>24</sup> In addition, it is a common condition in the so called “terminal” kidney disease of different etiologies and can result from aging.<sup>25</sup>

**Figure 3 -** Distribution of immunofluorescence findings.

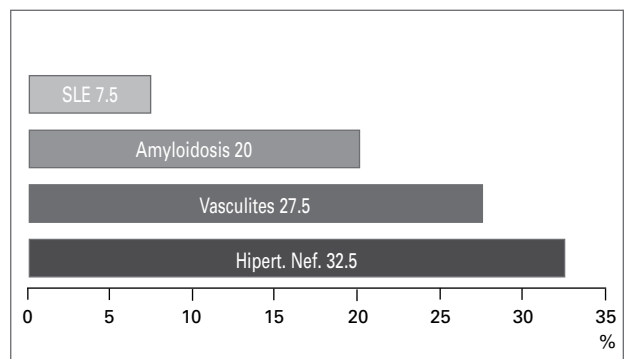


**Figure 4.** Frequency of primary glomerulopathies (n = 51).



MesPGN: Mesangioproliferative glomerulonephritis; IgAN: IgA nephropathy; ADGN: acute diffuse glomerulonephritis; MCD: Minimal change disease; FSGS: Focal segmental glomerulosclerosis; MN: Membranous nephropathy.

**Figure 5.** Frequency of secondary kidney diseases (n = 40).



Vasculites are very frequent in the elderly population. Furci *et al.*<sup>26</sup> have reported a 10% prevalence, which is four times greater than that in the adult. In our study, we found a similar percentage (9.7% of the cases), which was also observed in other studies.<sup>2,6,15</sup>

Although considered rare in the elderly population, not exceeding 4%, FSGS has also reached almost 10% of the elderly biopsies in our study, maybe because that is the most frequent glomerular disease in both regions here assessed.<sup>22,27</sup>

Contrary to most studies showing a high percentage of amyloidosis, in ours, only 7% of the biopsy reports had that diagnosis, despite the high number of nephrotic elderly (32.7% of the population). A Korean series has also diagnosed a reduced number of cases of amyloidosis in the elderly, not exceeding 6%.<sup>6</sup>

Aiming at assessing the usefulness of the kidney biopsy in that group, we observed that in 53.5% of our cases a therapeutic intervention would be necessary. Nair *et al.*<sup>12</sup>, studying a population over the age of 80 years, have reported 40% of diagnoses with consequent therapeutic indication. It is worth emphasizing that the decision of initiating or not an intervention in that group of patients should be very cautious, always considering the comorbidities that limit the choice of more aggressive therapies. On the other hand, even for patients whose histopathological diagnosis can not alter management, the information about prognosis can be fundamental to prevent unnecessary and even deleterious empirical treatments.

In conclusion, kidney biopsy in the elderly provides important information about diagnosis and prognosis in different clinical presentations, mainly when investigating nephrotic syndrome and acute kidney failure. In addition, advanced age by itself should not induce reluctance to perform kidney biopsy. Considering the greater tendency to longevity, further studies in this area should be encouraged, aiming at guiding not only nephrologists, but also internists, so that morbidity and mortality in the elderly can be prevented, and treatment become more effective.

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