Epidemiological analysis of the main diseases associated with patients with glomerulopathies diagnosed by biopsy in a university hospital in Minas Gerais

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ABSTRACT

Introduction: The kidney diseases most frequently diagnosed by biopsy are glomerulopathies. The epidemiological study of these diseases makes it possible to verify their distribution pattern in the population and their main etiologies, contributing to the decision on prevention and treatment strategies. **Objective**: To verify the diagnostic results of individuals who underwent renal biopsy in a university hospital in Belo Horizonte-MG, to evaluate the main associated comorbidities and outcomes. **Method:** This is an observational and cross-sectional study, with data obtained through the evaluation of the medical records of all patients who underwent renal biopsy in a university hospital between 2021 and 2022. Results: From the statistical analysis of the medical records of the 94 patients, a higher prevalence was observed in the results of Interstitial Fibrosis, Tubular Atrophy, and Focal and Segmental Glomerulosclerosis. The comorbidities that stood out as most prevalent were hypertension and diabetes. The computation of the incidence in the CKDEPI staging showed a higher frequency mainly in Stages 4 and 5, which allows us to infer that most of the individuals in the research are in more advanced stages of chronic kidney disease. **Conclusion**: The results showed that most patients studied, with an average age of 43 years, are allocated to more advanced stages of chronic kidney disease, thus requiring more elaborate care for possible bone complications and anemia. Such research was considerable to clarify the profile of patients with glomerulopathies who underwent biopsy in a public hospital in Belo Horizonte and their possible associated comorbidities.

Keywords: Glomerulonephritis, Diagnostics; Biopsy; Comorbidity

INTRODUCTION

Chronic Kidney Disease (CKD) is considered a public health problem worldwide. In Brazil, glomerulopathies are the third cause of end-stage chronic kidney disease, responsible for 11% of dialysis patients and 27.5% of transplants performed[1]. Currently, the incidence and prevalence of renal function failure are increasing, and the prognosis is still unfavorable[2]. Glomerular disease can result from many hereditary or acquired disorders and manifests in many ways. The main signs and symptoms are proteinuria of glomerular origin, glomerular hema-

turia, glomerular cylindruria, variable arterial hypertension, congestive states with the presence of edema and serous effusions, which can lead to acute renal failure (ARF) or end-stage renal disease[3]. Renal biopsy is constantly essential to diagnose the underlying pathology in patients with suspected glomerular disease, especially in those with nephrotic syndrome or suspected glomerulonephritis.[4] Rarely, a biopsy cannot be performed or is unnecessary to ensure a diagnosis. Numerous factors can lead to glomerular dysfunction and the symptoms manifested depend on the associated injury mechanism. For example, podocyte dysfunction can occur in genetic pathologies, affecting key basal membrane proteins, such as collagen IV mutations in Alport syndrome.[4] In diseases such as minimal change nephropathy and focal segmental glomerulosclerosis (FSGS), putative circulating factors are believed to affect podocyte function directly and lead to proteinuria.[5,6] In diabetes mellitus and amyloidosis, there is mechanical rupture of the glomerulus due to the accumulation of normal or abnormal proteins in the capillary loops of the glomerulus and mesangium.[5,7] In conditions such as systemic lupus erythematosus, immune-mediated kidney injury is caused by the deposition of circulating immune complexes. Finally, activated neutrophils and macrophages can directly damage the glomerulus in diseases such as vasculitis associated with cytoplasmic antineutrophil antibodies.[8,9] Manifestations associated with glomerular disease include hematuria and/or proteinuria, and renal failure, in addition to other symptoms such as hypertension, edema, hypercoagulability, and systemic findings.[4] Glomerular syndromes are typically classified based on the pattern of urinary abnormalities, the existence of systemic features, and the degree of renal failure. Nephrotic syndrome and glomerulonephritis are the most common presentations of glomerular disease. In nephrotic syndrome, loss of plasma proteins without inflammation is the main pathogenic mechanism. On the other hand, in glomerulonephritis, inflammation within the glomerulus leads not only to the passage of plasma proteins but also of inflammatory cells (leukocytes) and erythrocytes into the renal tubule. These classifications, however, are not exclusive, as some conditions can present with both patterns and some disorders (for example, lupus nephritis) can progress from one pattern to another.[10] Thus, the epidemiological survey of glomerulopathies allows us to identify their prevalence and the main causative factors and serves as a basis for defining their clinical, laboratory, and histological characteristics in each region, assisting in prevention and treatment strategies.[11] The present study aimed to analyze the profile of patients who underwent a biopsy at the university hospital in the period between 2021 and 2022, checking the associated comorbidities, the result of the biopsy, classifying the stage of chronic kidney disease using the CKD-EPI calculator, in addition, to check the outcome after performing the biopsy.

METHOD

Design

A cross-sectional study was carried out based on the analysis of data collected from the medical records of 94 patients who underwent a kidney biopsy from January 2021 to December 2022 at a university hospital in Belo Horizonte.

Sample

The target population of this study included patients of both sexes over 18 years of age who underwent a kidney biopsy at a university hospital during that period. Data were collected through the physical and electronic medical records of the university hospital. All patients who received care during the research period and who were diagnosed or treated without the need for a kidney biopsy were excluded from the research, as well as those who refused to participate in the research.

Procedures and Instruments

The data was collected through access to the patients' electronic medical records, with the Informed Consent Form being waived, as this data continued to be analyzed anonymously, with only the patient's medical record numbers being used. The variables were analyzed through medical records. Among them are continuous quantitative variables: age and duration of illness. The qualitative variables are gender, biopsy result, clinical manifestation, evolution, and calculation of the CKD-EPI. The CKD-EPI is an equation that seeks to correlate the patient's glomerular filtration rate with their age, sex, and baseline serum creatinine, allowing the degree of CKD to be estimated.[13]

Statistical Analysis

The statistical tests used were: the Wilcoxon test, Fisher's exact test, and Chi-square test of independence. These are statistical tests that can be used to evaluate the statistical significance of differences between groups or variables. The Wilcoxon rank sum test is a non-parametric test that can be used to compare the distribution of two independent or paired samples. It is used when assumptions of the Student T test are not met, such as when samples are not normally distributed. The Wilcoxon test is based on the sum of the ranks of each observation in the two samples and provides a measure of the statistical significance of the difference between the samples. Fisher's exact test is used to evaluate the statistical significance of an association between two categorical variables. It is used when the sample size is small, and the assumptions of the Chi-Square test are not met. Fisher's test is based on the exact probability distribution of the number of observations in each category and provides a measure of the statistical significance of the association between variables. The Chi-Square test of independence was also used, which is a test used to evaluate the statistical significance of an association between two categorical variables. The Chi-Square test is used when the sample size is large enough to meet its assumptions. It compares the observed and expected frequencies in each category, providing a measure of the statistical significance of the association between the variables. This test is especially useful when there are more than two categories in each variable and the association between them is not linear.

All ethical precepts involving scientific research were followed, guaranteeing privacy, secrecy, and confidentiality. No volunteer was identified at any stage of the study, and only the medical record number was used to ensure that they were not evaluated in duplicate. The present study was approved by the Ethics and Research Committee, CAAE 65061022.3.0000.5134

Results

The average value of the ages found is 43 years with an associated standard deviation of 15.59 years, indicating a relative variability around the average value of 35%. The data description table presented the median age as 42 years old, with the first quartile being 28 years old and the third quartile being 57 years old. Furthermore, it was possible to notice that the total number of male respondents was 51% while the percentage of women was 49%. Among the biopsy results, it was observed that the highest percentage was concentrated in Interstitial Fibrosis and Tubular Atrophy, at 23% of the occurrences, followed by Focal and Segmental Glomerulosclerosis at 19%. The length of illness had an average value of 6.68 years with a median of 5 years. Among the clinical manifestations, 40% are associated with Nephritic Syndrome while 28% are associated with Nephrotic Syndrome. Among the associated comorbidities, around 87% of patients have previous comorbidities.

Table 1: Demographic profile and clinical characteristics of patients who underwent biopsy at the university hospital between 2021 and 2022 (n=94).

Characteristics	N = 94[1]
AGE	43 (32, 57)
GENDER	
Female	46 (49%)
Male	48 (51%)
BIOPSY RESULT	
Interstitial Fibrosis and Tubular Atrophy	22 (23%)
Focal and Segmental Glomerulosclerosis	18 (19%)
IgA Nephropathy	13 (14%)
Lupus Nephritis	12 (13%)
Membranous Glomerulopathy	8 (8.5%)
Tubular Necrosis	8 (8.5%)
Diabetic Nephropathy	6 (6.4%)
Membranoproliferative Glomerulonephritis	4 (4.3%)
Crescentic Glomerulonephritis form Pauci-Immune	3 (3.2%)
TIME OF ILLNESS	4 years (mean)
CLINICAL MANIFESTATION	
Mixed Syndrome	18 (19%)
Nephritic Syndrome	40 (43%)
Nephrotic Syndrome	36 (38%)
COMORBIDITY	
No	11 (12%)
Yes	83 (88%)
Hypertension	
No	28 (30%)
Yes	66 (70%)
Diabetes	
No	72 (77%)
Yes	22 (23%)
Dyslipidemia	
No	74 (79%)
Yes	20 (21%)
Lupus	
No	86 (91%)
Yes	8 (8.5%)
EVOLUTION	
Hospital Discharge and outpatient follow-up	50 (53%)
Death	3 (3.2%)
Loss of Follow-up	10 (11%)
Kidney Transplant	16 (17%)
Kidney Replacement Therapy	15 (16%)
CKD EPI	
Classification 1 (>90)	10 (11%)
Classification 2 (60 a 89)	8 (8.5%)
Classification 3 (30 a 59)	20 (21%)
Classification 4 (15 a 29)	25 (27%)
Classification 5 (<15)	31 (33%)

.1Median (AIQ); n (%)

It is observed from the data shown in the table that there was no predominance of sex in the involvement of kidney pathologies. The average time with the disease was 4 years, with some cases having an evolution of less than 1 year and others with follow-up for more than 15 years, with a median of 5 years.

The comorbidities described in the study that appeared more regularly were hypertension, diabetes, and dyslipidemia, however, it should not be forgotten

that there were other concomitant illnesses, such as Systemic Lupus Erythematosus.

It is noted that more than half of the patients were discharged from the hospital, with a significant number of individuals undergoing Renal Replacement Therapy or Kidney Transplantation.

In the CKD EPI analysis, it is considered that around 60% of patients are in the terminal phase of chronic kidney disease (CKD). Due to this renal failure, glomerular filtration is replaced by dialysis (peritoneal or hemodialysis) while a donor is not found to perform the Kidney Transplant.

Based on the data in the table, it is observed that most of the studied population is under 45 years old. These individuals had a higher prevalence in Stages 4 and 5 in the CKD EPI Staging. The data computed from patients over 45 years old showed an approximately homogeneous distribution, apart from Stage 2, with only 3 representatives.

Table 2: Data crossing between CKD EPI Stages, patient gender, duration of illness, and average age of patients.

Characteristics	N	Total, N = 94[1]	CKD EPI Classification 1 (>90), N = 10[1]	Classification 2 (60 a 89), N = 8[1]	CKD EPI Classification 3 (30 a 59), N = 20[1]	Classification 4 (15 a 29), N = 25[1]	Classification 5 (<15), N = 31[1]	Valuep[2]
Class_Age	94							0.5
Over 45 years old		41 (44%)	7 (70%)	3 (38%)	9 (45%)	9 (36%)	13 (42%)	
Under 45 years old		53 (56%)	3 (30%)	5 (62%)	11 (55%)	16 (64%)	18 (58%)	

DISCUSSION

Renal biopsy has proven to be one of the best diagnostic methods for glomerular, tubulointerstitial, and vascular diseases, helping to determine the patient's prognosis and the best therapeutic approach.[14] Regarding the biopsy result, there was a greater frequency of Interstitial Fibrosis and Tubular Atrophy, along with Focal and Segmental Glomerulosclerosis (FSGS), a disease that is the most common etiology of nephrotic syndrome in adults.[12] Among the comorbidities associated with kidney pathologies found in the research, the presence of hypertension was noted in more than 60 patients evaluated in the study.

Through a detailed analysis of the results, it is possible to assess the prevalence of glomerulopathies and the main illnesses associated with them. The main findings in the biopsies, as evidenced, were interstitial fibrosis and tubular atrophy; focal and segmental glomerulosclerosis (GEFS), and IgA nephropathy.

Interstitial fibrosis and tubular atrophy correspond to classic changes in Interstitial Nephritis, in which there is an inflammatory infiltration in the renal interstitial (acute or chronic), which can be caused by an autoimmune disease, such as systemic lupus erythematosus (SLE), sarcoidosis and Sjogren's Syndrome, due to the use of medications, such as beta-lactams and non-steroidal anti-inflammatory drugs (NSAIDs), or due to infections, such as Legionellosis, Leptospirosis or Tuberculosis.[15] The symptoms presented depend on the etiology but lead to a decline in renal function.[16] A comparison with another study carried out in the state of Paraná, in 2011, confirmed tubulointerstitial nephropathy as the main finding in patients undergoing renal biopsy.[17]

The second main finding was Focal and Segmental Glomerulosclerosis (FSGS), which is the most common Nephrotic Syndrome in adults.[18] It consists of a podocyte lesion, with reductions in the podocyte processes, which leads to sclerosis of part of the glomerulus (segmental) and only some glomeruli (focal) in renal biopsy. It can be primary (idiopathic) or secondary to various conditions, such as HIV, and heroin use, among others. It is a classic nephrotic syndrome, with massive proteinuria, hypoalbuminemia, peripheral edema, and loss of renal function.[19,20]

The third most common result was IgA Nephropathy, a primary (idiopathic) glomerulonephritis, characterized by the deposit of IgA in the mesangium. The clinical presentation is quite variable, with microscopic and asymptomatic hematuria, macroscopic hematuria, nephrotic syndrome, and even rapidly progressive glomerulonephritis.[19] The most common pattern is alternation between macroscopic hematuria and periods of remission. Generally, periods of relapse are related to upper respiratory tract infections.

Regarding the association between glomerulopathies and the presence of comorbidities, 83% of patients with positive biopsies for glomerular diseases had some underlying disease. The highlight was Systemic Arterial Hypertension (SAH), present in 70% of patients. SAH is considered both a risk factor for kidney disease and a consequence of it, which worsens the prognosis of glomerulopathy. Blood pressure must be constantly monitored and treatment with non-pharmacological and pharmacological measures must be instituted.[20]

Another condition that is significantly present is Diabetes Mellitus, which was diagnosed in 23% of patients, which may be, the cause of glomerulopathy (diabetic nephropathy) or may be associated with other conditions that lead to glomerular disease.[21]

Regarding evolution, it was noted that most patients (53%) were discharged from the hospital and followed up on an outpatient basis. Another important portion, however, underwent Renal Replacement Therapy (RRT) (17%), with hemodialysis or peritoneal dialysis, and another portion had to undergo kidney transplantation (16%), which shows a relevant number of people with a terminal kidney.

The CKD-EPI is a tool that allows estimations of the glomerular filtration rate (GFR) in adults, using the following parameters: sex, race, age, and creatinemia. It was used in the research to evaluate the stage of chronic kidney disease presented by the patient, which implies the prognosis and the treatment instituted.[22] The data analysis was that 33% of biopsies belonged to stage 5 (GFR less than 15 mL/min/1.73m²), while 27% belonged to stage 4 (GFR between 29 and 15 mL/min/1.73m²), which already indicated an advanced disease at the time of the examination. In stage 4, in addition to closer monitoring of the patient, with regular exams and control of sodium and protein intake, referral to a reference service for catheter implantation is already indicated. In stage 5, RRT is indicated at levels below 10 mL/min/1.73m² of GFR and

in diabetics and people under 18 years, at levels below 15 mL/min/1.73m², or kidney transplantation.[22]

It is necessary to emphasize that CKD, in addition to its renal consequences, also has systemic repercussions, such as normocytic and normochromic anemia due to deficiency in the production of erythropoietin.[23] Furthermore, there are changes in bone remodeling due to the influence of parathyroid hormone, vitamin D deficiency (which is responsible for the absorption of calcium and phosphorus in the intestine), aluminum intoxication, generating a counterbalance in the activities of osteoclasts and osteoblasts, and causing demineralization bone.[24] Therefore, in addition to the comorbidities that generate CKD, it is essential to evaluate the impacts resulting from the disease for greater survival of the dialysis patient.

CONCLUSION

The epidemiological survey carried out in the study of glomerulopathies made it possible to identify which pathologies were most prevalent in the hospital where the research was carried out, along with the main associated comorbidities. There is still a significant number of patients affected by kidney disease. In the patients studied, it is clear that a large proportion of these individuals are under 45 years of age and that 58% of this population evaluated had renal replacement therapy as an outcome, which significantly impacts the quality of life and in some cases can even impair functionality. In older patients, an unfavorable result was also presented concerning disease follow-up. To avoid unfavorable developments, requiring renal replacement therapy or kidney transplantation, preventive measures must be taken, such as regular physical activity, a healthy diet, and stopping smoking and alcohol consumption.

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