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Research Article

Evaluation of Kidney Biopsies Performed in Patients Followed Up in the Nephrology Department of Our Hospital

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Abstract

Objectives: Renal biopsy plays a critical role in the diagnosis, prognosis and treatment management of renal parenchymal diseases. The aim of this study was to evaluate the clinicopathologic and laboratory characteristics of renal biopsies.

Methods: A total of 150 renal biopsies performed in the Nephrology Clinic of Bakırköy Dr. Sadi Konuk Training and Research Hospital between 2015 and 2017 were retrospectively evaluated. Biopsies of patients under 18 years of age, transplant kidney biopsies, biopsies without sufficient number of glomeruli for pathologic evaluation and biopsies evaluated in different pathology laboratories were excluded. Age, gender, laboratory data, indications for renal biopsy, histopathologic diagnosis and comorbidities of the patients were obtained from patient files and medical record system. These data were evaluated internally and comparatively.

Results: Among the patients who underwent renal biopsy, 44.67% were female and the male/female ratio was 1.23:1. The mean age of the patients was 45.73±14.98 years (18-80 years). The most common indication for biopsy was nephrotic proteinuria (33.33%). The most common pathology in all age and gender groups was primary glomerulonephritis with 67.33%. The most common primary glomerular diseases were focal segmental glomerulosclerosis (FSGS) (41.58%), IgA nephropathy (24.75%) and membranous glomerulonephritis (MGN) (17.82%). The most common cause of secondary glomerulonephritis was amyloidosis (50%).

Conclusion: In this study, all indications for biopsy were evaluated. Our study presents results consistent with the local and national literature, but also reveals regional differences.

Keywords: Renal biopsy, glomerulonephritis, nephrotic proteinuria

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The rising prevalence of end-stage renal disease (ESRD) with concomitant high morbidity and mortality has reached alarming levels worldwide. Although new treatment strategies for ESRD are promising, early diagnosis of chronic kidney disease (CKD), identification and treatment of risk factors for progression to ESRD are of great importance for both patient health and national economy.[1-5] Therefore, it is very beneficial to diagnose and start treatment before ESRD develops. At this stage, renal biopsy gains great importance. Kidney biopsy is accepted as the main method for definitive diagnosis of some renal diseases, determination of prognosis and selection of treatment modality.[6-8]

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Indications for renal biopsy vary between clinics. Glomerular diseases are the leading diseases diagnosed by renal biopsy and are classified as primary and secondary in terms of etiologic causes. Primary glomerular diseases are defined as diseases in which glomeruli are solely or predominantly involved without a known systemic disease or agent (such as drugs, infections, genetic and metabolic diseases). Diseases in which glomerular injury occurs as an organ involvement of a systemic disease or agent are categorized under the title of secondary glomerular diseases. Among both primary and secondary glomerular diseases, the most common type of disease is glomerulonephritis (GN), which is a non-bacterial inflammation of the glomeruli. Chronic GNs are the 3rd most common cause of CKD in Turkey.[9] In patients with suspected glomerular disease, renal biopsy should be performed without delay if there is no contraindication.

Information on the epidemiology of renal diseases has largely been obtained from renal biopsy records. We aimed to evaluate renal biopsies performed in our center in terms of clinicopathologic and laboratory characteristics and to compare them in terms of demographic data, biopsy indications, pathologic diagnoses, laboratory results and comorbidities.

Methods

This retrospective study included 150 patients who underwent renal biopsy in the Nephrology Clinic of Bakırköy Dr. Sadi Konuk Training and Research Hospital between 2015 and 2017. Biopsies of patients under 18 years of age, transplant kidney biopsies, kidney samples without sufficient number of glomeruli for pathologic evaluation, biopsy samples with insufficient clinical information and biopsies evaluated in different pathology laboratories were excluded from the study. Age, gender, laboratory data, indications for renal biopsy, histopathologic diagnosis and comorbidities of the patients were obtained from patient files and medical record system. Diabetes mellitus (DM), hypertension (HT), collagen tissue disease (CTD), coronary artery disease (CAD), familial Mediterranean fever (FMF) and CKD were investigated as comorbidities. Patients were evaluated according to demographic, clinical and laboratory data as well as biopsy indications and pathologic diagnoses. Patients were divided into 3 groups according to age: <40 years, 40-60 years, >60 years. Laboratory data, biopsy indications and pathologic diagnoses were compared according to gender and age groups.

Statistical Analysis

Frequency and percentage values were given for categorical variables. Mean, standard deviation, median, minimum and maximum values were given for continuous variables. Normal distribution of continuous variables was tested by Kolmogorov Smirnov test. Chi-square analysis and One sample Chi-square test were applied for the relationships between categorical variables. Where appropriate, categorical variables were evaluated with Fisher exact and Fisher Freeman Halton Test. Independent sample t test was used for continuous independent two-group comparisons with normal distribution and one-way analysis of variance (ANOVA) was used for comparisons of more than two independent groups. For variables that did not fulfill the assumption of normal distribution, Kruskal Wallis H test was used for comparisons of more than two independent groups. Bonferroni Dunn Multiple Comparison test was applied to determine the source of the significant difference. $p<0.05$ was considered statistically significant. Analyses were performed with NCSS 11 (Number Cruncher Statistical System, 2017 Statistical Software) Program.

Results

A total of 150 patients, 44.67% were female and 55.33% were male. The male/female ratio was 1.23:1. The mean age of the women was 46.18±15.61 years and the mean age of the men was 45.36±14.53 years. When evaluated according to age groups, 36.67% were below the age of 40 years, 42.67% were between the ages of 40-60 years and 20.67% were above the age of 60 years.

When the patients were evaluated in terms of comorbid diseases, 62 (41.33%) had HT, 25 (16.67%) DM, 8 (5.33%) CAD, 7 (4.67%) FMF, 10 (6.67%) CKD and 11 (7.33%) CVD. The distribution of comorbid diseases was similar in men and women, with HT ranking first and DM ranking second (Table 1).

The mean creatinine at initial presentation was 2.69 mg/dl serum albumin 3.33 g/dl urinary proteinuria 3645.09 mg/day.

The most common indication for biopsy was nephrotic proteinuria (50 patients; 33.33%). Other indications for biopsy were unexplained renal failure in 37 patients (24.67%), asymptomatic urinary findings in 35 patients (23.33%), ne-

Table 1. Distribution of additional diseases in patients

	Total, n (%)	Women, n (%)	Men, n (%)	p
HT	62 (41.33)	29 (43.28)	33 (39.76)	0.663
DM	25 (16.67)	12 (17.91)	13 (15.66)	0.713
CAD	8 (5.53)	4 (5.97)	4 (4.82)	1*
FMF	7 (4.67)	2 (2.99)	5 (6.02)	0.461*
CKD	10 (6.67)	2 (2.99)	8 (9.64)	0.186*
CTD	11 (7.33)	6 (8.96)	5 (6.02)	0.541*

HT: Hypertension; DM: Diabetes mellitus; CAD: Coronary artery disease; FMF: Familial Mediterranean fever; CKD: Chronic kidney disease; CTD: Collagen tissue disease; Chi-square test; *Fisher's Exact Test.

phritic proteinuria in 19 patients (12.67%), and isolated hematuria in 9 patients (6%). Two of the patients who underwent biopsy for unexplained renal failure had acute kidney injury in the background of CKD. When the indications for biopsy were evaluated according to gender, there was no difference in the indications for biopsy between men and women (p=0.461) (Table 2).

When the indications for biopsy were evaluated according to age groups, nephrotic proteinuria and unexplained renal failure were most common between the ages of 40 and 60 years, whereas nephritic proteinuria and isolated hematuria were seen below the age of 40 years. Isolated hematuria was the least common indication for biopsy in all three groups. There was no difference between age groups in terms of biopsy indications (p=0.793) (Table 3).

No statistically significant difference was found when biopsy indications were evaluated according to comorbidities (Table 4).

When the pathology results of renal biopsy were evaluated, primary GN was the most common (67.33%) and CKD was the least common (1.34%) (Fig. 1). There was no difference between pathology results according to gender and age groups (p=0.262; p=0.138). Primary GNs were more common in both sexes and age groups. Primary GNs were most common under the age of 40 years, while secondary GNs and tubulointerstitial nephritis were most common between the ages of 40 and 60 years.

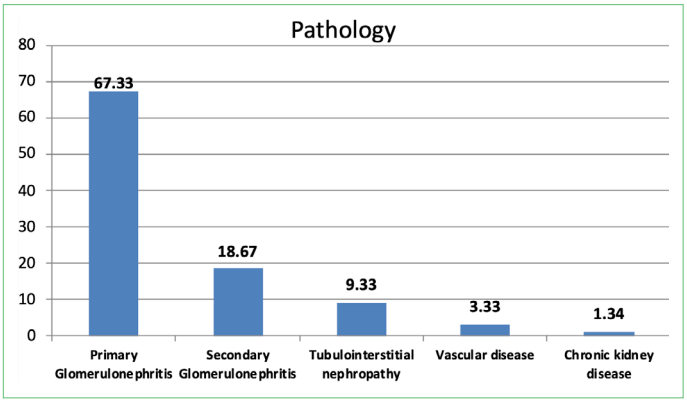

Figure 1. Percentage distribution of kidney biopsy pathology results.

Table 2. Biopsy indications of patients and distribution of biopsy indications according to gender

	Nephrotic proteinuria, n (%)	Nephritic proteinuria, n (%)	Asymptomatic urine findings, n (%)	Unexplained kidney failure, n (%)	Isolated hematuria, n (%)	p
All patients	50 (33.33)	19 (12.67)	35 (23.33)	37 (24.67)	9 (6)	0.461
Women	20 (40)	6 (31.58)	20 (57.14)	17 (45.95)	4 (44.44)	
Men	30 (60)	13 (68.42)	15 (42.86)	20 (54.05)	5 (55.56)	

Table 3. Biopsy indications according to age groups

Age	Nephrotic proteinuria, n (%)	Nephritic proteinuria, n (%)	Asymptomatic urine findings, n (%)	Unexplained kidney failure, n (%)	Isolated hematuria n (%)	p
<40	18 (36)	9 (47.37)	14 (40)	10 (27.03)	4 (44.44)	0.793
40-60	24 (48)	7 (36.84)	14 (40)	16 (43.24)	3 (33.33)	
>60	8 (16)	3 (15.79)	7 (20)	11 (29.73)	2 (22.22)	

Table 4. Biopsy indications according to co-morbidities

	Nephrotic proteinuria, n (%)	Nephritic proteinuria, n (%)	Asymptomatic urine findings, n (%)	Unexplained kidney failure, n (%)	Isolated hematuria, n (%)	p
HT	19 (38)	7 (36.84)	16 (45.71)	16 (43.24)	4 (44.44)	0.944
DM	10 (20)	3 (15.79)	5 (14.29)	6 (16.22)	1 (11.11)	0.977
CAD	4 (8)	0 (0)	1 (2.86)	2 (5.41)	1 (11.11)	0.571
FMF	3 (6)	1 (5.26)	2 (5.71)	0 (0)	1 (11.11)	0.361
CKD	3 (6)	2 (10.53)	3 (8.57)	2 (5.41)	0 (0)	0.871
CDT	3 (6)	1 (5.26)	4 (11.43)	3 (8.11)	0 (0)	0.858

HT: Hypertension; DM: Diabetes mellitus; CAD: Coronary artery disease; FMF: Familial Mediterranean fever; CKD: Chronic kidney disease; CTD: Collagen tissue disease.

When primary GNs were evaluated, a significant difference was observed in the distribution of pathologic diagnosis ($p<0.001$). Among primary GNs, FSGS was the most common (n=42; 41.58%), followed by IgA nephropathy (n=25; 25%) (Fig. 2). When evaluated according to gender, focal segmental glomerulosclerosis (FSGS) was the most common.

When secondary GNs were analyzed, amyloidosis was the most common with 50% (n=14). Diabetic nephropathy (n=7) and lupus nephritis (n=5) had similar rates, while light chain nephropathy was the least common (Fig. 3). When secondary GNs were evaluated according to gender, amyloidosis was most common in women and diabetic nephropathy was most common in men. According to age groups, lupus nephritis was the most common under 40 years of age, amyloidosis was the most common between 40-60 years of age and above 60 years of age.

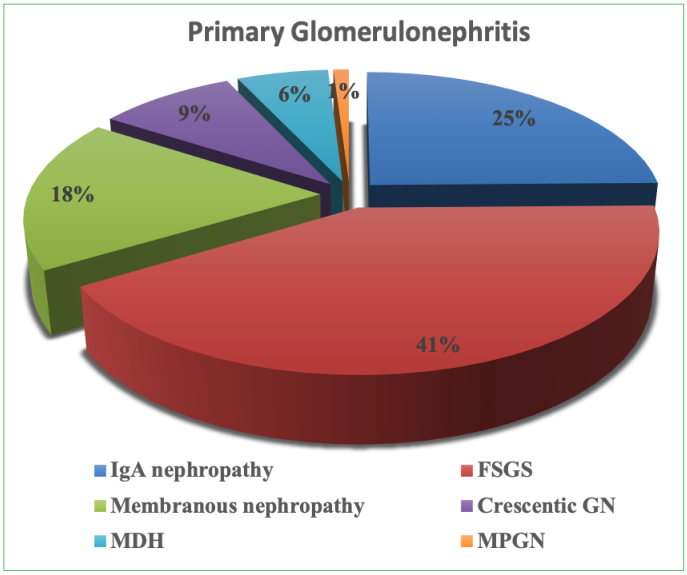

Figure 2. Distribution of pathologies that cause primary glomerulonephritis.

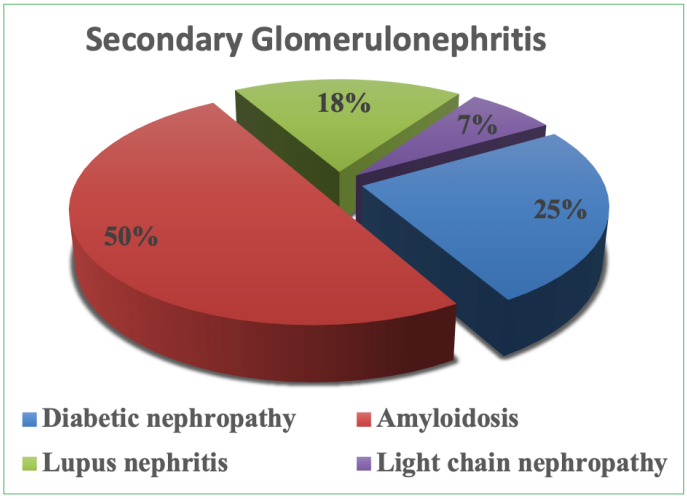

Figure 3. Distribution of secondary glomerulonephritis.

Acute tubular necrosis (ATN) was the most common tubulointerstitial disease. ATN was seen with equal frequency in both sexes and was most common between 40-60 years of age. HT nephropathy was seen with similar frequency in both sexes and most commonly over 60 years of age.

Discussion

The most common indication for renal biopsy in our study was nephrotic syndrome. Biopsies were performed more frequently in males than females. When we looked at the diagnoses, FSGS was the most common primary GN. IgA nephropathy was the second most common primary GN. The most common cause of secondary GNs was amyloidosis. Diabetic nephropathy and lupus nephritis were other common pathologies among secondary GNs. Especially lupus nephritis is common in the younger age group, whereas diabetic nephropathy is more prominent in the older age group. In our study, we observed that the prevalence of primary GNs was significantly correlated with age. IgA nephropathy was more common in patients under 40 years of age, while FSGS was more common in patients under 60 years of age.

Indications for renal biopsy vary between clinics. In a study conducted in Italy between 1996 and 2000 in which 14607 patients were evaluated, asymptomatic urinalysis disorder (UAD) was found to be the most common indication for biopsy.[10] Similarly, in a study conducted in Japan between 2007 and 2008, in which 2400 patients were evaluated, the most common indication for biopsy was found to be AIB.[11] In studies conducted in Spain,[12] Czech Republic[13] and Brazil,[14] the most common indication for biopsy was nephrotic syndrome. In our country, according to the data of the Glomerular Diseases Study Group of the Turkish Society of Nephrology (TND), the most common indication for renal biopsy is nephrotic syndrome with 57.8%.[15] In our study, the most common indication for renal biopsy was nephrotic syndrome in accordance with most studies in the literature. The reason why nephrotic syndrome was the most common indication for biopsy in many studies may be that patients presented after clinical findings related to proteinuria at nephrotic level. The fact that AIB is the most common indication for biopsy in some countries may be explained by the use of complete urinalysis as a screening method in some centers and more renal biopsies in cases of asymptomatic proteinuria or hematuria.

When we look at the incidence of diagnoses obtained by renal biopsy in the literature, FSGS was found to be the most common primary GN in a study conducted in India between 2012 and 2015.[16] In a study conducted in Brazil, FSGS was the most common primary GN.[14] In the same study, mem-

branous GN (MGN) and IgA nephropathy were the other common pathologic findings. In studies reported from Europe and Asia, IgA nephropathy was the most common primary GN.[10, 11, 13, 17-21] In some studies, conducted in our country, FSGS was shown to be the most common primary GN, similar to our study.[4-6] FSGS is a disease that is generally observed from childhood to adolescence, but it is also an important pathology in adults. However, IgA nephropathy also stands out as an important pathologic finding. In our study, IgA nephropathy was found to be the second most common primary GN. In the literature, it has been reported that the frequency of IgA nephropathy is increasing and this may be related to the more widespread use of immunofluorescence examinations. These differences between countries may be related to genetic, socioeconomic, environmental factors, differences in biopsy indications and obesity.

Secondary GNs occur due to glomerular injury when a systemic disease or agent affects the kidneys. In a study conducted in Italy, primary GNs were observed in 64.3% and secondary GNs in 24.7%.[10] In a study conducted in Brazil in which 2086 cases were examined, primary GN was found in 54.2% and secondary GN in 34.2%[14] In some studies in which the causes of secondary GN were evaluated, the most common cause was reported to be lupus nephritis[13, 14] and DM in others.[11] In studies conducted by Hür et al.[22] and Pişkinpaşa et al.[23] from our country, amyloidosis was observed as the most common cause. Secondary GNs were found to be proportionally lower in our study when compared with large study series. This result may be due to the fact that we perform fewer renal biopsies in diabetic patients in our clinic. The most common cause of secondary GNs was amyloidosis. It is known that amyloidosis is more common in our country, especially due to FMF. In addition, diabetic nephropathy and lupus nephritis are other common pathologies among secondary GNs. Especially lupus nephritis is common in the younger age group, while diabetic nephropathy is more prominent in the older age group. This is a reflection of the prevalence of diabetes and the impact of lupus disease in our country.

The effect of demographic factors such as age and gender on renal diseases is a frequently emphasized issue in the literature. When the pathologic diagnoses of the patients were evaluated according to age, the frequency of MGN was found to be high in patients older than 65 years in studies conducted in England, Czech Republic, Italy and Spain.[10, 12, 13, 17] In our study, no significant difference was observed between age groups in MGN. However, there was a correlation with age in the incidence of IgA nephropathy and FSGS. These findings, in parallel with other studies in the literature, show that glomerular diseases exhibit a changing distribution with age.

Although our study provides valuable results regarding renal biopsy outcomes, it has some limitations. First, since our study has a single-center and retrospective design, the generalizability of the data may be limited. More comprehensive analyses with data from different regions and centers may provide more comprehensive results on the distribution of glomerular diseases. Second, indications for renal biopsy may vary depending on the clinical practices and patient selection criteria of the centers. In particular, the frequency of biopsy in patients with AIB may vary from center to center and this may lead to underestimation of the frequency of some pathologies. Third, the pathologic diagnoses obtained in the study exclude cases that could not be diagnosed in patients who did not undergo renal biopsy; therefore, the study cannot accurately reflect the true prevalence of glomerular disease. Finally, data on the long-term prognosis and treatment response of patients could not be evaluated in this study. In future studies, prospective and multicenter databases and studies involving large patient populations will contribute to the diagnosis, treatment and prognosis processes of glomerular diseases.

In conclusion, we presented a comparative analysis of the demographic characteristics, indications for biopsy and pathologic diagnoses of patients undergoing renal biopsy. Our findings show that nephrotic syndrome is the most common indication for biopsy, while FSGS and IgA nephropathy are the most common primary glomerular diseases. Systemic diseases such as amyloidosis, lupus nephritis and diabetic nephropathy are the most common secondary glomerular diseases. Demographic factors such as age and gender were observed to play an important role in the distribution of glomerular diseases. This study once again emphasizes that renal biopsy is a critical method in the accurate diagnosis of glomerular diseases. However, since indications for biopsy may change over time, it is important to establish and update renal biopsy databases in local centers and on a national scale. Such databases will enable more accurate monitoring of renal diseases, guide treatment processes and improve clinical management.

Disclosures

Ethics Committee Approval: Bakırköy Dr. Sadi Konuk Training and Research Hospital Clinical Research Ethics Committee, Protocol code: 2017/163, Date: 19.06.2017.

Peer-review: Externally peer-reviewed.

Conflict of Interest: None declared.

Authorship Contributions: Concept – N.S., M.Y.; Design – N.S.; Supervision – M.Y.; Materials – N.S.; Data collection and/or processing – N.S., M.Y.; Analysis and/or interpretation – N.S.; Literature search – N.S.; Writing – N.S., M.Y.; Critical review – N.S.

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