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Clinicopathological evaluation of our patients with ultrasound assisted percutaneous kidney biopsy

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ABSTRACT

Aim: This study aims to determine the frequency of kidney diseases based on histological diagnosis and to evaluate the relationship between clinical and histopathological findings in patients undergoing percutaneous kidney biopsy for various indications.

Material and Method: In this cross-sectional study, demographic, anthropometric and laboratory data of the patients were obtained retrospectively from medical files and computer records. Biopsy indications and histopathological diagnoses (primary glomerular diseases, secondary glomerular diseases, tubulointerstitial diseases and other causes) of the patients were examined.

Results: Of 103 patients, 57 (55.3%) were male and 46 (44.7%) were female. The mean age of the patients was 44.67±15.29 years. The most common biopsy indication was hematuria+proteinuria+renal dysfunction (n=28, 27.2%). The most common pathology in histopathological diagnoses was primary glomerular diseases (56.3%), the most common diagnosis was IgAN (n=16, 15.5%). Tubulointerstitial diseases were seen more frequently in the 60 years and older group. (n=4, 25%). The most common cause of secondary glomerulonephritis was AA amyloidosis. The number of tubular disorders increased with advanced age.

Conclusion: In our center, renal biopsy was performed most frequently with the combination of proteinuria, hematuria, and renal dysfunction. The most common histopathological result was primary glomerulonephritis, in which IgAN took the first place.

Keywords: glomerulonephritis, histopathological diagnoses, renal biopsy

INTRODUCTION

Percutaneous kidney biopsy has a crucial role in diagnosing kidney diseases and guiding treatment in nephrology practice. It is the gold standard method in the diagnosis of renal parenchymal diseases, in predicting the course of the disease and in detecting the need for treatment (1). Today, it is performed with automatic or semi-automatic needles under the guidance of ultrasonography (USG), and the incidence of major complications is fairly low (2).

The most common indications for percutaneous kidney biopsy are nephrotic syndrome, nephritic syndrome, isolated microscopic hematuria, asymptomatic urinalysis abnormalities, acute kidney injury, suspected transplant kidney rejection, multisystemic diseases with renal involvement, and unidentified loss of kidney function (3). Diagnoses identified in kidney biopsies differ corresponding to the age, gender of the patients, whether they have native or transplanted kidneys, biopsy indications of centers, and race and geographical distribution (4).

This study purposes to determine the frequency of kidney diseases based on histological diagnosis and to assess the relationship between clinical and histopathological findings in patients who underwent percutaneous kidney biopsy for various indications in our center.

MATERIAL AND METHOD

This study was initiated after the approval of the Dışkapı Yıldırım Beyazıt Training and Resarch Hospital Ethics Committee (Date: 11/01/2021, Decision No: 102/01), and all procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

In this retrospective and cross-sectional study, the frequency of kidney diseases identified in patients who had percutaneous kidney biopsy with different indications and the relations between clinical and histopathological findings were examined. Informed consent form was obtained from all patients before the procedure.

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The Demographic, anthropometric, and lab data of the subjects were acquired retrospectively from medical files and computer registries.

Biopsy indications were microscopic hematuria (>2 erythrocytes per amplification field in urine sediment examination), proteinuria (>150 mg/day), renal dysfunction (unidentified loss of glomerular filtration rate), and post-treatment control (relapsed or treatment-resistant disease).

Percutaneous kidney biopsies were performed by the Interventional Radiology Unit or our nephrology team, using semi-automatic 16G and 18G biopsy needles, in the prone position, with at least 2 samples taken. The samples were placed on gauze impregnated with saline and delivered to Hacettepe University of Medicine Pathology Department within one hour in Petri dishes. A 2–4 mm long renal cortical tissue sample was reserved for examination and frozen sections were taken from these samples with a cryostat. IgG, IgA, IgM, C3, C1q, fibrinogen, kappa, and lambda dyes were applied by immunofluorescence method and evaluated with special filters in the immunofluorescence microscope. The remaining biopsy specimen was fixed with 10% formaldehyde. After routine tissue follow-up, 4µm-thick sections of tissue samples embedded in paraffin blocks were stained with Hematoxylin & Eosin, Periodic Acid Schiff, Masson Trichrome, Congo Red, and Methenamine Silver dyes and evaluated under a light microscope.

Biopsy results were classified as 1-Primary glomerular diseases [immunoglobulin A nephropathy (IgAN), focal segmental glomerulosclerosis (FSGS), membranous glomerulonephropathy (MGN), minimal change disease (MCD), membranoproliferative glomerulonephritis (MPGN), crescentic glomerulonephritis (anti-neutrophil cytoplasmic antibodies (ANCA)-associated vasculitis and anti-glomerular basement membrane antibody glomerulonephritis), post-infectious glomerulonephritis (PIGN)], 2-Secondary glomerular diseases [AA amyloidosis, systemic lupus erythematosus nephritis, diabetic nephropathy, monoclonal immunoglobulin deposition disease (MIDD), vascular renal damage (thrombotic microangiopathies)]; 3-Tubulointerstitial diseases (acute tubulointerstitial nephritis) (ATIN), 4-Hereditary renal diseases, 5-Chronic changes and 6-Others (oxalate nephropathy, nephrocalcinosis, undetermined diagnoses).

Statistical Analysis

Statistical analyzes were performed using the 25th version of the Statistical Package for the Social Sciences software (SPSS Inc., Chicago, IL, USA). The distribution of numerical variables was assessed using the Kolmogorov-Smirnov test. Normally distributed continuous data were compared with Student's t-test, and the results of the tests were given as mean values±standard deviation (SD). Abnormally distributed data were compared with the Mann-Whitney U test and results were presented as median and interquartile range. Comparisons of categorical variables were made using the Chi-square test and Fisher's exact test; results were presented as numbers and percentages.

RESULTS

All adult patients (n=112) who had a renal percutaneous biopsy in our nephrology clinic between November 2018 and March 2020 were assessed for the study. Patients whose biopsy specimens were technically inadequate for histopathological assessment (n=3) and patients who had biopsy from a transplanted kidney (n=6) were omitted from the study. 103 patients were recruited for the study eventually. Of the patients included in this study, 57 (55.3%) were male and 46 (44.7%) were female. The mean age of the patients was 44.67±15.29 years. Of these, 42 were under the age of 40, 45 were between the ages of 40-60, and 16 were aged 60 and over. In the patient groups separated according to biopsy indications, the mean age of those who underwent biopsy with the indication of isolated renal dysfunction was 61.75±17.37 years, while the mean age of the other groups ranged from 35.65±15.20 to 49.00±17.26 years (**Table 1**).

Table 1. Age and gender distribution of patients according to biopsy indications

		Gender		
Biopsy indication	**n=103**	**Male (n=57)**	**Female (n=46)**	**Age**
Hematuria, proteinuria and kidney dysfunction	28 (27.2%)	19 (67.9%)	9 (32.1%)	49.00±17.26
Proteinuria and kidney dysfunction	26 (25.2%)	14 (53.8%)	12 (46.2%)	44.58±12.77
Isolated proteinuria	25 (24.3%)	11 (44%)	14 (56%)	43.88±11.70
Nephrotic range proteinuria	13 (12.6%)	9 (69.2%)	4 (30.8%)	11.90
Non-nephrotic proteinuria	12 (11.7%)	2 (16.7%)	10 (83.3%)	44.08±11.99
Hematuria and proteinuria	17 (16.5%)	11 (64.7%)	6 (35.3%)	35.65±15.20
Isolated kidney dysfunction	4 (3.9%)	1 (25%)	3 (75%)	61.75±17.37
Re-biopsy after treatment	3 (2.9%)	1 (33.3%)	2 (66.7%)	40.00±18.68

Categorical variables are shown as frequency and percentages.

The most common biopsy indication in our study population was hematuria+proteinuria+renal dysfunction (n=28, 27.2%). This indication was also

the most common among men (n=19, 33.3%). Other biopsy indications were proteinuria+renal dysfunction (n=26, 25.2%), isolated proteinuria (n=25, 24.3%), hematuria+proteinuria (n=17, 16.5%), isolated renal dysfunction (n=4, 3.9%) and post-treatment control (n=3, 2.9%) (**Table 1**). None of the patients underwent biopsy, with indications of either isolated hematuria or hematuria+renal dysfunction.

In the analysis in which histopathological diagnoses were grouped, primary glomerular diseases had the highest rate (n=58, 56.3%). Among these, the most common diagnosis was IgAN (n=16, 15.5%). The most common primary glomerular disease identified in men was IgAN (n=12, 21.1%), while in women it was FSGS (n=7, 15.2%). When the distribution is made according to age groups, IgAN in patients younger than 40 years of age (n=9, 21.4%), FSGS in the 41-59 age group (n=11, 24.4%), and ATIN in patients 60 years and older (n=4, 25%) were the most common pathologies (**Table 2**).

The histopathological distribution of the patients according to biopsy indications is shown in **Table 3**. Hematuria+proteinuria (n=5, 38.5%) for MGN, hematuria+proteinuria+kidney dysfunction (n=7, 43.8%) for IgAN, nephrotic range proteinuria (n=6, 40%) for FSGS, nephrotic range proteinuria (n=3, 60 %) for MCD. The most common indication (n=6, 85.7%) was hematuria+proteinuria+renal dysfunction in patients with the diagnosis of crescentic glomerulonephritis.

DISCUSSION

This study intends to estimate out the frequency of renal diseases based on histological diagnosis and to evaluate the relationship between clinical and histopathological findings in patients who underwent percutaneous kidney biopsy for various indications in our center.

We considered the data from 103 patients who went through percutaneous biopsy of their native kidney over a course of almost one and a half years. The mean age of the patients at the point of diagnosis was 44.67±15.29 years, and 55.3% were male. These results were comparable to the data in the studies of Piskinpaşa et al. (5) and O'Shaughnessy et al. (6).

Although the indications for kidney biopsy differ according to race, geography and centers, the most common indication reported to date is proteinuria (7-10). In our study, unlike other studies, the most common biopsy indication was hematuria+proteinuria+renal dysfunction. When we reevaluate the biopsy indications in our study, it is noteworthy that only 7 patients did not have proteinuria. Our most common indication for biopsy may have appeared to be different, as our classification was different from other studies.

According to the 2020 Registry report of the Turkish Society of Nephrology, the most common cause of chronic renal failure in patients undergoing dialysis after diabetes and hypertension is glomerulonephritis (11). Glomerular diseases are the leading diseases diagnosed by percutaneous kidney biopsy.

Table 2. Distribution of histopathological diagnoses by gender and age

		Gender		Age groups		
Diagnosis	**Total (n=103)**	**Male (n=57)**	**Female (n=46)**	**≤40 year old (n=42)**	**40-59 (n=45)**	**≥60 year old (n=16)**
IgAN	16 (15.5%)	12 (21.1%)	4 (8.7%)	9 (21.4%)	5 (11.1%)	2 (12.5%)
FSGS	15 (14.6)	8 (14%)	7 (15.2%)	3 (7.1%)	11 (24.4%)	1 (6.3%)
MGN	13 (12.6)	9 (15.8%)	4 (8.7%)	4 (9.5%)	7 (15. 6%)	2 (12.5%)
ATIN	10 (9.7%)	4 (7.0%)	6 (13.0%)	5 (11.9%)	1 (2.2%)	4 (25%)
Chronic changes	11 (10.7%)	7 (12.3%)	4 (8.7%)	4 (9.5%)	6 (13.3%)	1 (6.3%)
Crescentic glomerulonephritis	7 (6.8%)	6 (10.5%)	1 (2.2%)	1 (2.1%)	3 (6.7%)	3 (18.8%)
AA amyloidosis	7 (6.8%)	2 (3.5%)	5 (10.9%)	3 (7.1%)	3 (6.7%)	1 (6.3%)
MCD	5 (4.9%)	3 (5.3%)	2 (4.3%)	2 (4.8%)	3 (6.7%)	-
Hereditary renal diseases	4 (3.9%)	1 (1.8%)	3 (6.5%)	2 (4.8%)	2 (4.4%)	-
Lupus nephritis	4 (3.9%)		4 (8.7%)	4 (9.5%)	-	-
Diabetic nephropaty	3 (2.9%)	2 (3.5%)	1 (2.2%)	1 (2.4%)	2 (4.4%)	-
MPGN	2 (1.9%)	1 (1.8%)	1 (2.2%)	2 (4.8%)	-	-
Nephrocalcinosis	1 (1.0%)	1 (1.8%)	-	1 (2.4%)	-	-
Oxalate nephropathy	1 (1.0%)	-	1 (2.2%)	-	-	1 (6.3%)
MIDD	1 (1.0%)		1 (2.2%)	-	1 (2.2%)	-
TMA	1 (1.0%)	-	1 (2.2%)	-	-	1 (6.3%)
PIGN	1 (1.0%)	-	1 (2.2%)	-	1 (2.2%)	-
Undetermined diagnoses	1 (1.0%)	1 (1.8%)	-	1 (2.4%)	-	-

Categorical variables are shown as frequency and percentages. Abbreviations: IgAN: immunoglobulin A nephropathy, FSGS: focal segmental glomerulosclerosis, MGN: membranous glomerulophropathy, ATIN: acute tubulointerstitial nephritis, AA: amyloid A, MCD: minimal change disease, MPGN: membranoproliferative glomerulonephritis, MIDD: monoclonal immunoglobulin deposition disease, TMA: thrombotic microangiopathy, PIGN: postenfectious glomerulonephritis

Table 3. Distribution of histopathological diagnoses of patients according to biopsy indications

	Biopsy Indication							
	Isolated proteinuria							
Diagnoses	**Non-nephrotic proteinuria**	**Nephrotic range proteinuria**	**Hematuria and proteinuria**	**Isolated kidney dysfunction**	**Proteinuria and kidney dysfunction**	**Hematuria, proteinuria and kidney dysfunction**	**Re-biopsy after treatment**	**Total**
MGN	2 (15.4%)	3 (23.1%)	5 (38.5%)	-	2 (15.4%)	1 (7.7%)	-	13 (100%)
IGAN	2 (12.5%)	-	3 (18.8%)	-	4 (25%)	7 (43.8%)	-	16 (100%)
FSGS	3 (20%)	6 (40%)	2 (13.3%)	-	3 (20%)	1 (6.7%)	-	15 (100%)
MCD	-	3 (60%)	-	-	2 (40%)	-	-	5 (100%)
MPGN	-	-	1 (50%)	-	-	1 (50%)	-	2 (100%)
Crescentic glomerulonephritis	-	-		-	-	6 (85.7%)	1 (14.3%)	7 (100%)
Hereditary renal diseases	1 (25%)	-	2 (50%)	-	-	1 (25%)	-	4 (100%)
ATIN	-	-	2 (20%)	2 (20%)	4 (40%)	2 (20%)	-	10 (100%)
AA amyloidosis	1 (14.3%)	-	-	-	3 (42.9%)	3 (42.9%)	-	7 (100%)
Lupus nephritis	1 (25%)	-	1 (25%)	-	-	1 (25%)	1 (25%)	4 (100%)
Diabetic nephropaty	1 (33.3%)	1 (33.3%)	-	-	1 (33.3%)	-	-	3 (100%)
MIDD	-	-	-	-	-	1 (100%)	-	1 (100%)
TMA	-	-	-	1 (100%)	-	-	-	1 (100%)
PIGN	-	-	-	-	-	1 (100%)	-	1 (100%)
Chronic changes					7 (63.6%)	3 (37.3%)	1 (9.1%)	11 (100%)
Undetermined diagnoses	-	-	1 (100%)		-	-	-	1 (100%)
Oxalate nephropathy	-	-	-	1 (50%)	-	-	-	1 (100%)
Nephrocalcinosis	1 (50%)	-	-					1 (100%)

Categorical variables are shown as frequency and percentages. Abbreviations: IgAN: immunoglobulin A nephropathy, FSGS: focally segmental glomerulosclerosis, MGN: membranous glomerulophropathy, ATIN: acute tubulointerstitial nephritis, MCD: minimal change disease, MPGN: membranoproliferative glomerulonephritis, MIDD: monoclonal immunoglobulin deposition disease, TMA: thrombotic microangiopathy, PIGN: postenfectious glomerulonephritis AA: amyloid A

We detected glomerular disease in approximately 70% of all cases in our study group. 56.3% of glomerulonephritis was due to primary causes and 13.6% to secondary causes. Among primary GN, the most common cause was IgAN (15.5%). This result was similar to the results previously reported in Czechia (9), Italy (4), France (12), England (13), USA (14), China (15), Korea (16) and our country (17). According to the very recently published KDIGO Clinical Practice Guidelines for Glomerular Diseases, IgAN is also the most common primary glomerular disease worldwide (18).

It was observed that there were differences in the pathological subtypes of glomerulonephritis according to age groups. The dominance of IgAN in the age group of 40 and below, of FSGS in the age group of 41-59, and of ATIN in the group of 60 and above was remarkable. In our analysis, as in similar studies (19), it was observed that the rate of renal tubular diseases increased while the rate of glomerular disease decreased as the mean age of the patients increased. The reason ATIN is frequently observed in the 60-year-old and older group may be the prevalence of over-the-counter drugs (especially analgesics) and herbal treatment used in this age group (20). In our study, data collection and analysis were not carried out in this direction. In the future, analyses that include data on drugs used and co-morbidities may provide clearer results.

In our study, the most common biopsy indication in patients diagnosed with MGN was hematuria+proteinuria. Although nephrotic syndrome is frequently seen in MGN, it should be kept in mind that 30-40% of it is accompanied by hematuria. (21).

In our study, AA amyloidosis was the first among secondary GNs. Although studies reporting lupus nephritis among the most common causes draw attention (12,22,23), there are also studies reporting AA amyloidosis (24). The geographic prevalence differences of diseases such as Familial Mediterranean Fever causing AA amyloidosis may contribute to these heterogeneous results.

The incidence of diabetic nephropathy may vary depending on the differences in kidney biopsy indications in diabetic patients. In our center, biopsy is not performed in diabetic cases with typical features of diabetic nephropathy, such as long-term DM, presence of DM-related microvascular complications such as diabetic retinopathy and neuropathy, and documented microalbuminuria-macroalbuminuria process. This approach may explain our low rate of diabetic nephropathy.

Study Limitations

The first is the evaluation of biopsy specimens only by light microscopy and immunofluorescence examination. Electron microscopic examination could not be performed. Secondly, the collection of cases from a single center resulted in a limited sample size.

CONCLUSION

In our center, the most common indication for kidney biopsy was proteinuria+hematuria+renal dysfunction, the most common primary glomerulopathy was IgAN, and the most common secondary glomerulopathy was AA amyloidosis. Tubular diseases were more common in advanced ages. We expect our findings will help us to build up faster and more accurate approaches to the target patient group.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was initiated with the approval of the Dışkapı Yıldırım Beyazıt Training and Research Hospital Ethics Committee (Date: 11.01.2021, Decision No: 102/01).

Informed Consent: Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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Author Contributions: All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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