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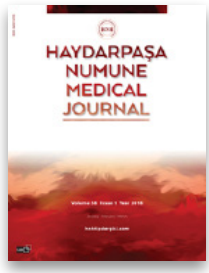

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ORIGINAL ARTICLE

Evaluation of Kidney Biopsies in Adults; 10 Years Single-Center Experience

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Abstract

Introduction: Kidney biopsy is a frequent method of assessing the cause, extent and sometimes the appropriate treatment response of renal parenchymal diseases. In this study, we evaluated the clinicopathologic features of kidney biopsy examinations performed in our center for 10 years.

Methods: A total of 532 native kidney biopsies performed in the adult age group between the years 2005-2014 in Haydarpaşa Training and Research Hospital were evaluated retrospectively. All biopsy specimens were examined by light microscopy and immunofluorescence by the same pathologist in the same laboratory.

Results: The mean age of the cases was 41.3±12.8 years (18-65 years) and the percentage of males was 52.3% (n=278). The most frequent biopsy indication for primary and secondary glomerulonephritis was nephrotic-range proteinuria. The most frequent histopathologic diagnoses were focal segmental glomerulosclerosis among primary glomerulonephritis and diabetic nephropathy among secondary glomerulonephritis.

Discussion and Conclusion: As a result of the evaluation of 10-year kidney biopsy series at our center, results which are in general compatible with the national and international literature have been obtained. We concluded that establishment of kidney biopsy databases both at local centers and at national scales would be beneficial in the evaluation of kidney diseases.

Keywords: Diabetic nephropathy; focal segmental glomerulosclerosis; glomerulonephritis; kidney biopsy, nephrotic syndrome.

Renal parenchymal diseases usually occur with general findings such as proteinuria and hematuria, and laboratory tests are often insufficient in the differential diagnosis. Because of these reasons, kidney biopsy is a frequently used method in nephrology practice. It is also a determinant for the stage of involvement, prognosis, and treatment to be given in some diseases such as immunoglobulin A nephropathy (IgAN) and lupus nephritis (LN)[1,2]. Nephritic syndrome, nephrotic syndrome, familial renal disease, renal transplant dysfunction, systemic disease with renal dysfunction, isolated proteinuria/hematuria and acute or chronic kidney disease of unknown etiology are main clinical indications for kidney biopsy[3].

The prevalence of renal parenchymal diseases that can be diagnosed with kidney biopsy may vary depending on factors such as geographical area, socioeconomic structure, race, and gender[4,5]. Therefore, kidney biopsy data analysis identifies regional epidemiological distributions of glomerular diseases and contributes to clinical evaluation. Kidney biopsy data have been analyzed in Turkey and in many different parts of the world and have been published in the lit-

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erature. In the present study, we evaluated the clinicopathologic and laboratory features of kidney biopsy examinations performed in our center for a duration of 10 years.

Materials and Methods

532 native kidney biopsies performed at the Haydarpasa Numune Training and Research Hospital between 2005 and 2014 were reviewed retrospectively. Age, gender, kidney biopsy indication, and histopathological diagnostic information were obtained from the medical record system. Before the biopsy, renal function tests, hemoglobin level, platelet count, prothrombin time and active partial thromboplastin time were checked and written consent was obtained from each patient. Using 16-18 G semi-automated needles with ultrasonography in biopsies, and by taking two core samples; biopsies sampled under 7 glomeruli, transplant kidney biopsies, biopsies of patients under 18 years and patients over 65 years of age, and biopsy samples with inadequate clinical information were excluded from the study. Samples that were examined by the same pathologist in the same laboratory with light microscopy and immunofluorescence methods were included in the study.

Indications for kidney biopsy as indicated by clinicians were classified as follows; 1- Unexplained renal failure (Acute kidney injury or chronic kidney disease (AKI was defined as a sudden increase (several days to weeks) in serum creatinine of ≥0.3mg/dl (≥26.4 μmoL/L) or ≥50% from baseline and/or reduction in urine output<0.5 ml/kg/hr for more than 6 hours) and CKD was considered when elevated serum creatinine persisted for >3 months.) 2- Nephritic syndrome (proteinuria >1.5 g/day in the presence of oedema or hypertension and erythrocyte cylinders in the urine), 3- Nephrotic range proteinuria (>3.5 gr/day), 4- Asymptomatic urine findings (non-nephrotic proteinuria and hematuria), 5- Isolated proteinuria (<3.5 gr/day and no hematuria), 6- Isolated hematuria (macroscopic and microscopic).

The pathological classification was divided into 5 groups; primary glomerulonephritis, secondary glomerulonephritis, tubulointerstitial diseases, vascular diseases, and others. Primary glomerulonephritis was classified as focal segmental glomerulosclerosis (FSGS), IgAN, membranous nephropathy (MN), minimal change disease (MCD), crescentic glomerulonephritis (CresGN), membranoproliferative glomerulonephritis (MPGN) and other glomerulonephritis (diffuse proliferative glomerulonephritis, endocapillary proliferative glomerulonephritis, IgM nephropathy, membranoproliferative nodular pattern, mesangioproliferative glomerulonephritis, postinfectious glomerulonephritis). Secondary glomerular diseases were classified as LN, diabetic nephropathy (DN), secondary amyloidosis (AA), plasma cell dyscrasias associated nephropathy (cast nephropathy/primary amyloidosis (AL)), cryoglobulinemia, and systemic vasculitis. Tubulointerstitial diseases were classified as acute tubular necrosis, acute tubulointerstitial nephritis, chronic tubulointerstitial nephritis, and chronic pyelonephritis. Vascular diseases were classified as hypertensive nephropathy, and thrombotic microangiopathy. Additionally, biopsy studies that were classified as normal biopsy findings, unidentified biopsy findings, hereditary renal diseases and end-stage renal disease were grouped separately.

Data obtained from patient files and hospital computer records were analyzed statistically with SPSS-18. Continuous variables are given as frequency, mean and standard deviation (mean ± standard deviation).

Results

Between 2005 and 2014, 1032 kidney biopsies were carried out at the Haydarpasa Numune Training and Research Hospital. A total of 532 kidney biopsies were evaluated retrospectively after biopsies that do not fit the study criteria were excluded from the study. Mean age of patients was 41.3±12.8 years (18-65 years), while 278 (52.3%) patients were male. Average serum creatinine level was calculated as 1.4±0.95 mg/dl, proteinuria as 4.6±1.91 gr/day and the mean number of glomeruli was 14.2±10.3.

Primary glomerulonephritis was the most common group of renal diseases (49.8%, n=265). Among other pathological classifications, frequency of secondary glomerulonephritis was 24.7%, frequency of unidentified renal parenchymal diseases was 7.8%, frequency of tubulointerstitial diseases was 5.6%, frequency of normal specimens was 5.5%, frequency of vascular diseases was 4.3%, frequency of end-stage renal disease was 1.9%, and frequency of hereditary diseases was 0.4% (Table 1).

Table 1. Pathological classification of kidney biopsies

Diagnosis	n	%
Primary glomerulonephritis	265	49.8
Secondary glomerulonephritis	132	24.7
Unidentified biopsy findings	41	7.8
Vascular diseases	23	4.3
Tubulointertisial diseases	30	5.6
Normal biopsy findings	29	5.5
End stage renal disease	10	1.9
Hereditary	2	0.4
Total	532	100

The most common biopsy indication for glomerulonephritis (primary and secondary) was nephrotic range proteinuria (54.2%). Other indications are, in descending order of frequency, unexplained renal failure (17.6 %), asymptomatic urine findings (13.3%), isolated proteinuria (11.3%), nephritic syndrome (3.3%) and isolated hematuria (0.3%) (Table 2).

Table 2. Biopsy indications for primary and secondary glomerulonephritis

Biyopsi Endikasyonları **Biopsy Indications**	**Histolojik Tanı** **Histological Diagnosis****	**n** **Number of patients**	**Ratio**
Nephrotic range proteinuria	FSGS	50	16.8
	MN	40	13.5
	AA	36	12.1
	DN	22	7.4
	MCD	19	6.4
	MPGN	15	5.1
	IgAN	13	4.4
	Other primary glomerulonephritis*	8	2.7
	LN	7	2.3
	CresGN	4	1.3
	Cryoglobulinemia	1	0.3
Renal Failure	DN	15	5.1
	IgAN	12	4.1
	FSGS	11	3.7
	CresGN	11	3.7
	Other primary glomerulonephritis*	5	1.7
	AA	6	2.1
	LN	3	1.1
	Systemic vasculitis	3	1.1
	Cast nephropathy/AL	3	1.1
	MPGN	1	0.3
Asymptomatic urine findings	IgAN	28	9.4
	LN	13	4.4
	FSGS	5	1.7
	Other primary glomerulonephritis*	3	1.1
	DN	2	0.6
	MCD	1	0.3
	Cryoglobulinemia	1	0.3
Isolated proteinuria	FSGS	14	4.7
	LN	10	8.1
	DN	7	2.3
	IgAN	4	1.3
	MN	4	1.3
	Other primary glomerulonephritis*	3	1.1
	AA	2	0.6
	MPGN	1	0.3
Nephritic Syndrome	CresGN	12	4.1
	Systemic vasculitis	1	0.3
Isolated hematuria	Other primary glomerulonephritis*	1	0.3
Total		397	100

FSGS: Focal segmental glomerulosclerosis, IgAN: IgA nephropathy, MN: Membranous nephropathy, CresGN: Crescentic glomerulonephritis, MCD: Minimal change disease, MPGN: Membranoproliferative glomerulonephritis, DN: Diabetic nephropathy, AA: Secondary amyloidosis, AL: Primary amyloidosis, LN: Lupus nephritis; * (Diffuse proliferative glomerulonephritis, endocapillary proliferative glomerulonephritis, IgM nephropathy, membranoproliferative nodular pattern, mesangioproliferative glomerulonephritis, postinfectious glomerulonephritis); **In this table, only biopsy indications of primary and secondary glomerulonephritis were evaluated.

Among primary glomerulonephritis, pathological diagnoses were FSGS (30.2%), IgAN (21.5%), MN (16.6%), CresGN (10.2%), MCD (7.5%), MPGN (6.4%) and others (7.5%), respectively (Table 3). 45% of FSGS diagnosed patients had massive proteinuria (>6 gr/day) and patients with non-nephrotic range proteinuria had renal failure (11 patients) and/or additional disease that may cause kidney disorder (13 patients) and/or hematuria (14 patients) (Tables 3, 4).

Among secondary glomerulonephritis, pathological diagnoses were; DN (34.8%), AA (33.3%), LN (25.9%), systemic vasculitis (3.1%), cast nephropathy (2.3%) and cryoglobulinemia (1.5%), respectively (Table 5). DN diagnosed patients with non-nephrotic range proteinuria had renal failure (13 patients) and/or additional disease that may cause kidney disorder (12 patients) and/or hematuria (12 patients) and massive proteinuria (> 6gr/day) was detected in 17 of 22 the patients with nephrotic range proteinuria (Table 6).

Table 3. Distribution of primary glomerulonephritis

Diagnosis	n	%
FSGS	80	30.2
IgAN	57	21.5
MN	44	16.6
CresGN	27	10.2
MCD	20	7.5
MPGN	17	6.4
Others*	20	7.5
Total	265	100

FSGS: Focal segmental glomerulosclerosis; IgAN: IgA nephropathy; MN: Membranous nephropathy; CresGN: Crescentic glomerulonephritis; MCD: Minimal change disease; MPGN: Membranoproliferative glomerulonephritis; * (Diffuse proliferative glomerulonephritis; endocapillary proliferative glomerulonephritis; IgM nephropathy, membranoproliferative nodular pattern; mesangioproliferative glomerulonephritis, postinfectious glomerulonephritis).

Table 4. Baseline characteristics of biopsy proven focal segmental glomerulosclerosis patients

Male/Female	40/40
Age (years)	40.7[1]
Blood Creatinine (mg/dl)	1.6[1]
Proteinuria (gr/day)	7.1[1]
Massive proteinuri (>6gr/day)	36
Hematuria[2] (n)	14
Additional disease that may cause kidney disorder[2] (n)	13
Renal failure[2] (n)	11

[1]median values are presented in the table; [2]patients with non-nephrotic range proteinuria.

Discussion

Kidney biopsy has taken its place at the center of nephrology practice since the middle of the 19th century[6] and has been developed in many aspects from the technical point of view and will continue to develop. Today, it is the most effective and reliable method for diagnosis of renal parenchymal diseases. In the present study, we evaluated the clinicopathological features of kidney biopsies performed in our center and provided comprehensive information about the incidence of kidney biopsy proven renal diseases during a period of 10 years in the western part of Turkey.

Although biopsy indications differ between centers, many studies have reported the most frequent indication of kidney biopsy as nephrotic-range proteinuria[7-12]. In a review that evaluates data from 25 centers in Turkey, the rate of kidney biopsy indication of nephrotic syndrome for primary glomerulonephritis was reported to be 57.8%[13]. In our study, the nephrotic syndrome was the most frequent biopsy indication for glomerulonephritis with a rate of 54.2%. The rate of kidney biopsy with nephrotic-range proteinuria indication for glomerulonephritis was reported

Table 5. Distribution of secondary glomerulonephritis

Diagnosis	n	%
DN	46	34.8
AA	44	33.3
LN	33	25.9
Systemic vasculitis	4	3.1
Cast nephropathy	3	2.3
Cryoglobulinemia	2	1.5
Total	132	100

DN: Diabetic nephropathy; AA: Secondary amyloidosis; AL: Primary amyloidosis; LN: Lupus nephritis.

Table 6. Baseline characteristics of biopsy proven diabetic nephropathy patients

Male/Female (n)	30/16
Age (years)	51.9[1]
Blood Creatinine (mg/dl)	1.7[1]
Proteinuria (gr/day)	4.7[1]
Massive proteinuri (>6 gr/day)	17
Renal failure[2] (n)	13
Additional disease that may cause kidney disorder[2] (n)	12
Hematuria[2] (n)	12

[1]median values are presented in the table; [2]patients with non-nephrotic range proteinuria.

to be between 31.5-64.5% in other studies conducted in Turkey, and MN, MCD, MPGN, DN and amyloidosis cases were the most frequent histopathological diagnoses in biopsies with nephrotic syndrome indications[14-16].

In our study, primary glomerulonephritis was the most frequent diagnosis for kidney biopsy, and FSGS was the most frequent pathological diagnosis with a rate of 30.2% among primary glomerulonephritis. Similarly, FSGS has been reported to be the most frequent diagnosis among primary glomerulonephritis in two studies that were conducted in Brazil and in Turkey[12,16]. It is known that the incidence of FSGS has increased throughout the world over the years, supporting these findings[17,18]. This may be due to increased incidence of adaptive FSGS secondary to chronic inflammation or obesity as well as increased awareness of FSGS. In our study, indication of kidney biopsy of FSGS group was massive proteinuria for approximately half of the patients which is more compatible with primary FSGS. However, there is no certainty regarding the subject due to both the complexity of the etiology of FSGS and the insufficiency of epidemiological studies. In our study, IgAN and MN were found as the second and third most frequent among primary glomerulonephritis, respectively. In the most comprehensive study conducted in Turkey that evaluates data from 25 centers, MN is the most frequent diagnosis among primary glomerulonephritis[13]. In studies conducted in European and Asian countries, IgAN is the most frequently detected primary glomerulonephritis[7-11,19,20]. In another study conducted in Turkey, IgAN is the most frequent primary glomerulonephritis[15].

Although none of the studies conducted in Turkey have identified DN as the most frequent secondary cause of glomerulonephritis in any series[13-16,21,22], DN is the most frequent pathological diagnosis among secondary glomerulonephritis with a rate of 34.8% in our study. Similar to our findings, studies that were conducted in Japan and Scotland reported DN as the most frequent secondary glomerulonephritis[7,8]. However, there are no standardized criteria for kidney biopsy in diabetic patients, but it has been reported in a study that evaluation of DN with only clinical findings may lead to misdiagnosis, and the gold standard for diagnosis may be the kidney biopsy[23]. In our study, 36.9% of DN diagnosed by kidney biopsy were performed to investigate the etiology of massive proteinuria, while the most of other biopsies in diabetic patients were made due to other reasons that complicate the diagnosis of DN.

AA and LN were the second and third most frequent secondary glomerulonephritis respectively after DN. Amyloidosis was the most frequent secondary glomerulonephritis in two studies conducted in Turkey[16,24]. AA cases can be explained by the high incidence of familial Mediterranean fever in Turkey[25]. In Asian and European countries, LN is the most frequent cause of secondary glomerulonephritis[7,9,12,19,20]. Similarly, in two other studies conducted in Turkey, the most common secondary glomerular disease was LN[14,15].

As a result of the evaluation of the kidney biopsy series at our center from last 10-years, results which are in general compatible with the national and international literature have been obtained. But the prevalence of diseases that can be diagnosed by kidney biopsy may change over time. In our study, the frequency of FSGS among primary glomerulonephritis, and the frequency of DN among secondary glomerulonephritis are more frequent in our series compared to the other studies performed in Turkey and are notable. Therefore, the creation and updating of kidney biopsy databases at both local centers and at national scales would be useful for guidance in the evaluation of kidney diseases.

Ethical Committee Approval: Retrospective study.

Peer-review: Externally peer-reviewed.

Authorship Contributions: Concept: M.T., U.K.; Design: M.T., S.A.; Data Collection or Processing: G.G., M.T..; Analysis or Interpretation: M.T., S.A., G.Ş.; Literature Search: M.T., S.A., G.Ş.; Writing: M.T., U.K., G.G.

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