

Clinical and histopathological analyses of kidney biopsies in a single center for 7 years

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Abstract

Kidney biopsy is the most important tool for diagnosing kidney disease and can be helpful in determining treatment and prognosis. Pathological spectra vary by country, region, race, sex, and age. We are the first to investigate the pathological spectrum of biopsy-proven kidney disease in Gyeongnam province of South Korea. We retrospectively analyzed 631 patients who underwent a kidney biopsy between 2013 and 2019 at Gyeongsang National University Hospital. The mean age of the 631 patients was 51.5 ± 18.1 years, and 361 patients (57.2%) were male. The mean estimated glomerular filtration rate by serum creatinine (Chronic Kidney Disease Epidemiology Collaboration [CKD-EPI]) was 68.0 ± 45.7 mL/min/1.73 m². The mean systolic blood pressure was higher in 2017, 2018, and 2019 than in 2013 ($P = .002$). Hypertension (47.4%) was the most common comorbid disease, followed by diabetes (18.2%) and dyslipidemia (10.9%). Common clinical syndromes at the time of biopsy were renal insufficiency (42.0%) and nephrotic syndrome (33.9%). The prevalence of primary and secondary glomerular disease and tubulointerstitial disease were 71.4%, 16.9%, and 5.4%, respectively. Immunoglobulin A nephropathy was the most common primary glomerular disease (34.9%). Diabetic nephropathy was the most common secondary glomerular disease, followed by lupus nephritis. Tubulointerstitial disease was underestimated, as in other reports. Our data can be a useful reference for diagnosing kidney disease and understanding the patients in our province.

Abbreviations: AKI = acute kidney injury, ATIN = acute tubulointerstitial nephritis, AUA = asymptomatic urinary abnormality, CKD = chronic kidney disease, CVA = cardio/cerebrovascular accident, DBP = diastolic blood pressure, DM = diabetic mellitus, DN = diabetic nephropathy, eGFR = estimated glomerular filtration rate, ESRD = end-stage renal disease, FSGS = focal segmental glomerulosclerosis, HT = hypertension, HT-N = hypertensive nephropathy, IgAN = immunoglobulin A nephropathy, IP = isolated proteinuria, LN = lupus nephritis, MAP = mean arterial pressure, MCD = minimal change disease, MIDD = monoclonal immunoglobulin deposition disease, MN = membranous nephropathy, MPGN = membranoproliferative glomerulonephritis, NS = nephrotic syndrome, RI = renal insufficiency, SBP = systolic blood pressure, SLE = systemic lupus erythematosus.

Keywords: glomerular disease, kidney biopsy, tubulointerstitial disease

1. Introduction

The incidence of chronic kidney disease (CKD) is increasing, and we are always interested in identifying and accurately diagnosing its various causes.^[1] In a previously reported Korean cohort study of kidney biopsies, the most common cause of CKD was glomerular disease, followed by diabetic nephropathy (DN), hypertensive nephropathy (HT-N), and polycystic kidney disease.^[2] Although diabetes and hypertension (HT) are the most common causes of CKD worldwide, glomerular diseases, infections, and environmental exposures such as air pollution and herbal medications are also common causes in Asia.^[3,4]

A kidney biopsy is one of the most important tools for diagnosing various types of kidney disease, whether the cause is primary, secondary, or hereditary. We can not only diagnose patients but also establish treatment directions and evaluate prognosis using the pathological findings obtained through a kidney biopsy.^[5]

Many researchers have analyzed the patterns of biopsy-proven glomerular disease. The resulting pathological spectra vary by country, region, race, sex, and age. In the past, membranous nephropathy (MN) was the most common glomerular disease in Europe,^[6] but in recent reports, immunoglobulin A nephropathy (IgAN) and focal segmental glomerulosclerosis (FSGS) have predominated in Europe. Lupus nephritis (LN) and FSGS were

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The datasets generated during and/or analyzed during the current study are not publicly available, but are available from the corresponding author on reasonable request.

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dominant in Latin America. In Asia, LN and IgAN were the most common glomerular diseases.^[7] MN was the most dominant in the United States in previous reports, but FSGS has recently been increasing and become a major cause of end-stage renal disease (ESRD).^[8] Membranoproliferative glomerulonephritis (MPGN) was the most common glomerular disease in South Africa.^[9] Those differences clearly indicate that geographical, social, and environmental differences affect the distribution of glomerular disease. In countries with large territories, such as China, regional differences can also exist. Two recently reported cohorts in China showed different results: IgAN was the most common glomerular disease in East China, but MN was the most common in Central China.^[10,11]

In past reports from various centers in South Korea, the most frequent glomerular disease was IgAN.^[12-15] According to data from the Korean National Statistical Office reported in 2021 (<https://jumin.mois.go.kr/>), Gyeongnam province is located in the southwestern part of Korea. It has one of the highest average age of the population in South Korea, and the proportion of the population aged over 65 years has been steadily increasing since 2000. Most centers that conducted studies similar to ours were in the central or southwestern area of Korea. Kidney biopsy results from the Gyeongnam cohort have not yet been analyzed. Therefore, we investigated the pathological spectrum of biopsy-proven kidney disease using a retrospective analysis of patients who underwent a kidney biopsy in a single center in Gyeongnam. We would like to compare our data with previous cohort studies in South Korea to determine whether our province has unique characteristics and reorganize the basis for treating patients with kidney disease.

2. Material and Methods

2.1. Study participants

This is retrospective observational study. We collected data from 691 patients who underwent a kidney biopsy between January

2013 and December 2019 in Gyeongsang National University Hospital (GNUH), which is the only tertiary national hospital in Gyeongnam province. After excluding patients younger than 18 and patients with transplanted kidneys, insufficient tissue, diagnosed 2 or more diseases, or missing data, 631 patients were included (Fig. 1). This study was approved by the Institutional Review Board (IRB) of GNUH (IRB number: 2020-06-007).

2.2. Kidney biopsy

We performed kidney biopsy in cases with clinical syndrome described in Table 1. Patients with rapidly progressive acute kidney injury (AKI) or CKD of unknown etiology were also included. In diabetic patients, kidney biopsy was considered when the disease progressed in an atypical course. All kidney tissue was obtained through ultrasound-guided percutaneous kidney needle biopsies by nephrologist. Two to 3 specimens were collected from one side of the kidney while the patient was lying in a prone position. The number of glomeruli was checked in real time by a pathologist to make sure that the tissue was suitable for examination. The basic tests performed to make an accurate diagnosis were light microscopy, electron microscopy, and immunofluorescence microscopy. However, when the sample was insufficient or the glomerulus was not sufficiently observed in the sample, electron microscopy and immunofluorescence microscopy could not be performed.

2.3. Clinical syndromes

At the time of the kidney biopsies, clinical syndromes were classified into 5 categories, as shown in Table 1. Renal insufficiency (RI) was reclassified into 2 categories, AKI and CKD,

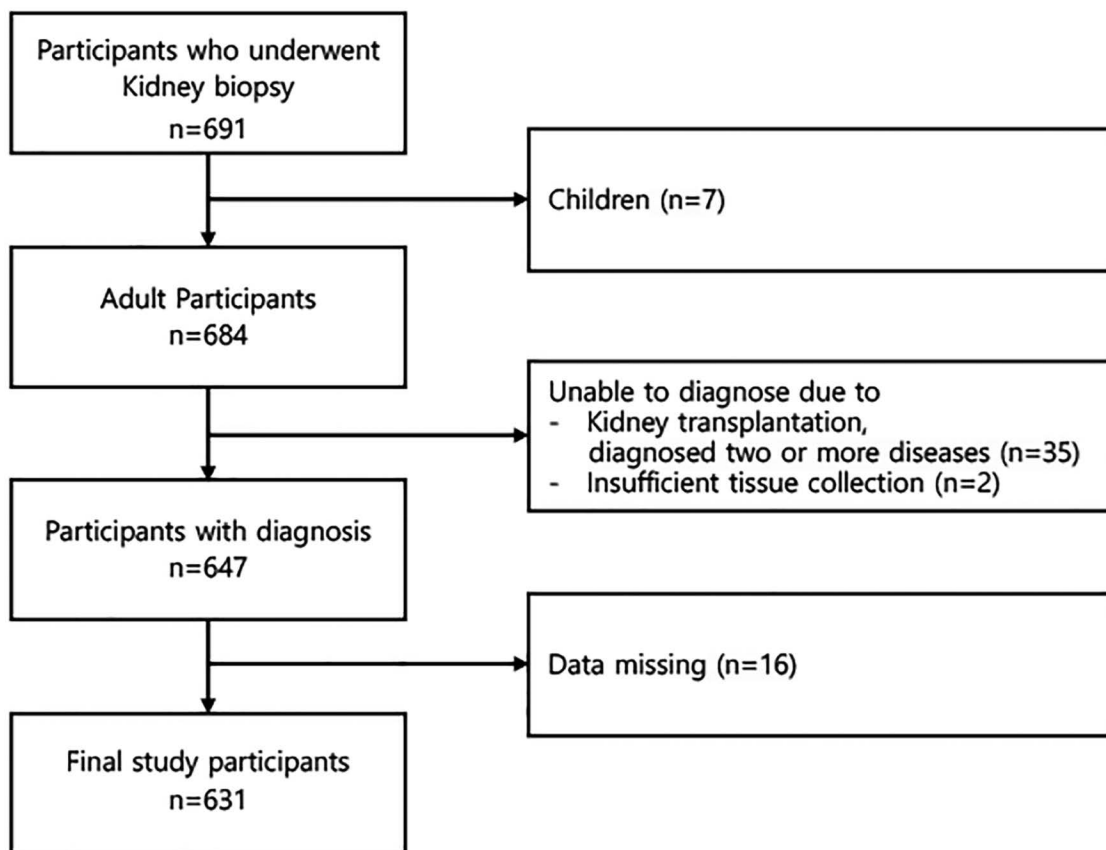


Figure 1. Flowchart of participant selection.

Table 1**Definition of clinical syndromes associated with glomerular disease.**

	Definition
AUA	Microscopic hematuria or subnephrotic proteinuria without clinical symptoms or signs
IP	Non-nephrotic range proteinuria without hematuria
NS	24-h urine protein ≥ 3.5 g or uPCR ≥ 3000 mg/mg with edema, hyperlipidemia, or hypoalbuminemia
RI	eGFR < 60 mL/min/1.73m ²

AUA = asymptomatic urinary abnormalities, eGFR = estimated glomerular filtration rate, IP = isolated proteinuria, NS = nephrotic syndrome, RI = renal insufficiency, uPCR = urine protein to creatinine ratio.

which were defined according to the Kidney Disease: Improving Global Outcomes (KDIGO) Clinical Practice Guidelines.^[16,17]

2.4. Pathological diagnoses

Pathological diagnoses were classified according to a recent classification system.^[18] Each pathologic diagnosis was divided into one of 7 categories: primary glomerular disease, secondary glomerular disease, tubulointerstitial disease (TID), vascular disease, hereditary congenital renal disease, ESRD, and other/miscellaneous (Table 2). We categorized 3 patients with mesangial proliferative glomerulonephritis as IgAN. One patient with C3 glomerulopathy was included in the MPGN category.

2.5. Demographics and laboratory findings

Age, sex, height, weight, systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), history of antihypertensive drugs, serum creatinine, serum albumin, the urine protein to creatinine ratio (uPCR, g/g), presence of hematuria, and serologic markers for glomerular disease were collected at the time of kidney biopsy.

Histories of diabetic mellitus (DM), HT, malignancy including various solid cancers and hematologic malignancies, cerebral or cardiovascular accident (CVA), viral hepatitis including hepatitis type B and C, and dyslipidemia were confirmed by referring to the hospitalization and medical records written at the time of admission for kidney biopsy. The estimated glomerular filtration rate (eGFR) was calculated using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) creatinine equation.^[19,20]

2.6. Statistical analysis

To compare variables among patient groups in different years, we performed Cochran-Armitage trend test for the categorical variables and the Jonckheere-Terpstra test for the continuous variables. All tests were 2 tailed, and a *P* value < 0.05 was considered statistically significant. We used R 4.0.3 (R Core Team, Vienna, Austria) for all statistical analyses and related graphics.

3. Results

3.1. Demographics of patients with kidney biopsy

The mean age of the 631 patients in our study population was 51.5 ± 18.1 years (Table 3). Three hundred sixty-one patients (57.2%) were male, and the mean age and sex did not differ significantly by year. The mean SBP was 138.8 ± 24.1 mm Hg. The mean SBP, DBP, MAP, and body mass index at the time of kidney biopsy had been on an increasing trend significantly since 2013.

Table 2**Classification of renal pathological diagnoses.**

Classification	Diagnosis
Primary glomerular disease	IgAN, including MsPGN
	FSGS
	MN
	MCD
	MPGN, including C3 glomerulopathy
Secondary glomerular disease	Crescentic GN
	DN
	LN
	HT-N
	HSP
Tubulointerstitial disease	Amyloidosis
	MIDD
	ATIN
	CTIN
Vascular disease	TMA
Hereditary congenital renal disease	TBMD
End-stage renal disease	Alport syndrome
	Advanced glomerulosclerosis; impossible to diagnose original renal disease
Other/miscellaneous	IgAN
	Idiopathic nodular glomerulosclerosis, acute pyelonephritis, no specific change

ATIN = acute tubulointerstitial nephritis, CTIN = chronic tubulointerstitial nephritis, DN = diabetic nephropathy, FSGS = focal segmental glomerulosclerosis, GN = glomerulonephritis, HSP = Henoch-Schönlein purpura, HT-N = hypertensive nephropathy, IgAN = immunoglobulin A nephropathy, LN = lupus nephritis, MCD = minimal change disease, MIDD = monoclonal immunoglobulin deposition disease, MN = membranous nephropathy, MPGN = membranoproliferative GN, MsPGN = mesangial proliferative GN, TBMD = thin basement membrane disease, TMA = thrombotic microangiopathy.

HT (47.4%) was the most common comorbidity, followed by DM (18.2%), dyslipidemia (10.9%), malignancy (7.0%), CVA (6.2%), and viral hepatitis (4.9%). The mean eGFR was 68.0 ± 45.7 mL/min/1.73 m². The most common clinical syndrome at the time of biopsy was RI (42.0%), followed by nephrotic syndrome (NS) (33.9%) and asymptomatic urinary abnormalities (AUA) (23.1%). Trend test showed that the ratio of AUA and RI decreased and that of NS increased by year, but the most common clinical syndrome was RI for 7 years (*P* = .005). AUA was the most common in patients aged 19 to 39 years (58.9%). NS, isolated proteinuria (IP), and RI were dominant in patients older than 60 years, respectively (Fig. 2).

3.2. Differences in clinical characteristics and eGFR according to pathological diagnosis

The prevalence of glomerular disease on kidney biopsy was 88.3% (557 patients), with the primary cause being dominant (450 patients, 71.4%) and the secondary cause being nondominant (107 patients, 16.9%). The prevalence of TID was 5.4% (34 patients) (Table 4).

Among the primary glomerular diseases, IgAN (34.9%) was the most common disease, followed by FSGS (17.1%). The mean age of IgAN and MPGN were 44.8 ± 16.4 years and 65.6 ± 12.7 years, respectively. The proportion of males in MN was 73.8% and females were the only predominant in MPGN (54.5%). The mean eGFR of crescentic glomerulonephritis (GN) and minimal change disease (MCD) were 17.2 ± 33.1 mL/min/1.73m² and 107.3 ± 51.0 mL/min/1.73m², respectively.

Among the secondary glomerular diseases, DN (6.0%) was the most common disease, followed by LN (4.3%) and HT-N (4.0%). The prevalence of monoclonal immunoglobulin deposition disease (MIDD) and Henoch-Schönlein purpura was 0.9% and 0.6%, respectively. The mean eGFR of DN and HT-N were 38.5 ± 24.2 mL/min/1.73m² and 38.9 ± 32.3 , mL/min/1.73m², respectively. The mean age of LN was 42.4 ± 15.1 years and females

Table 3

Demographic and clinical characteristics of patients undergoing renal biopsy by year.

Characteristics	2013 (N = 120)	2014 (N = 94)	2015 (N = 93)	2016 (N = 99)	2017 (N = 70)	2018 (N = 81)	2019 (N = 74)	Total (N = 631)	P value*
Age, year	48.2±18.9	54.3±17.5	52.2±17.5	50.3±19.5	51.3±17.7	52.0±18.4	53.2±16.1	51.5±18.1	.236
Male	66 (55.0)	57 (60.6)	55 (59.1)	60 (60.6)	36 (51.4)	44 (54.3)	43 (58.1)	361 (57.2)	.779
SBP, mm Hg	131.1±24.3	136.7±23.4	140.5±25.4	139.1±23.5	143.9±23.3	142.6±25.0	142.8±20.7	138.8±24.1	<.001
DBP, mm Hg	79.7±15.2	81.6±16.90	82.1±15.1	82.1±13.5	83.0±15.9	82.3±14.0	83.7±13.8	81.9±14.9	.020
MAP, mm Hg	96.8±17.2	100.0±18.3	101.5±17.0	101.1±15.8	103.3±16.8	102.4±16.1	103.4±14.8	100.9±16.8	<.001
BMI, kg/m ²	23.7±3.9	24.5±3.7	24.6±4.1	25.0±4.1	24.1±3.9	24.8±4.2	25.5±5.1	24.6±4.2	.019
eGFR, mL/min/1.73m ²	70.5±53.3	63.9±47.3	65.1±47.0	73.0±44.3	71.5±43.4	62.4±39.1	69.0±39.8	68.0±45.7	.508
Comorbidities									
HT	55 (45.8)	45 (47.9)	48 (51.6)	45 (45.5)	31 (44.3)	39 (48.1)	36 (48.6)	299 (47.4)	.918
DM	13 (10.8)	16 (17.0)	22 (23.7)	16 (16.2)	14 (20.0)	17 (21.0)	17 (23.0)	115 (18.2)	.040
Dyslipidemia	14 (11.7)	7 (7.4)	10 (10.8)	6 (6.1)	8 (11.4)	9 (11.1)	15 (20.3)	69 (10.9)	.107
Malignancy	9 (7.5)	10 (10.6)	4 (4.3)	3 (3.0)	4 (5.7)	5 (6.2)	9 (12.2)	44 (7.0)	.813
CVA	5 (4.2)	7 (7.4)	6 (6.5)	5 (5.1)	4 (5.7)	5 (6.2)	7 (9.5)	39 (6.2)	.342
Viral hepatitis	10 (8.3)	4 (4.3)	4 (4.3)	5 (5.1)	3 (4.3)	2 (2.5)	3 (4.1)	31 (4.9)	.124
Clinical syndrome									
AUA	39 (32.5)	16 (17.0)	25 (26.9)	28 (28.3)	16 (22.9)	11 (13.6)	11 (14.9)	146 (23.1)	.005
NS	31 (25.8)	37 (39.4)	27 (29.0)	28 (28.3)	31 (44.3)	30 (37.0)	30 (40.5)	214 (33.9)	
IP	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.2)	5 (6.8)	6 (1.0)	
RI	50 (41.7)	41 (43.6)	41 (44.1)	43 (43.5)	23 (32.9)	39 (48.1)	28 (37.9)	265 (42.0)	
AKI	20 (16.7)	36 (38.3)	33 (35.5)	35 (35.4)	20 (28.6)	32 (39.5)	24 (32.5)	200 (31.7)	
CKD	30 (25.0)	5 (5.3)	8 (8.6)	8 (8.1)	3 (4.3)	7 (8.6)	4 (5.4)	65 (10.3)	

Values are presented as mean ± SD or number (%).

AKI = acute kidney injury, AUA = asymptomatic urinary abnormality, BMI = body mass index, CKD = chronic kidney disease, CVA = cardio/cerebrovascular accident, DBP = diastolic blood pressure, DM = diabetic mellitus, eGFR = estimated glomerular filtration rate, HT = hypertension, IP = isolated proteinuria, MAP = mean arterial pressure, NS = nephrotic syndrome, RI = renal insufficiency, SBP = systolic blood pressure.

*P values were determined by Cochran-Armitage trend test for the categorical variables and the Jonckheere-Terpstra test for the continuous variables.

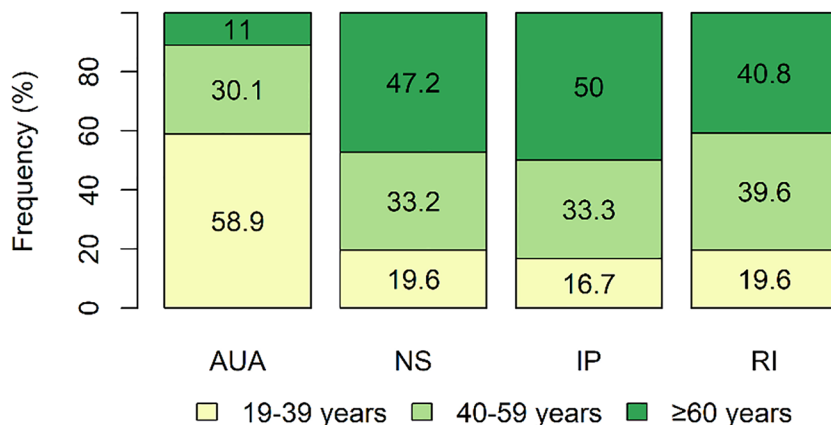


Figure 2. Age distributions according to clinical indications for renal biopsy. AUA = asymptomatic urinary abnormality, IP = isolated proteinuria, NS = nephrotic syndrome, RI = renal insufficiency.

were dominant (92.6%) in LN, and the mean eGFR of LN was 100.2±55.3 mL/min/1.73m². The mean age of MIDD and amyloidosis were 63.5±11.0 years and 62.9±7.6 years, respectively.

Figure 3 shows the distribution of pathological diagnoses by age (Supplementary Table S1, <http://links.lww.com/MD/G962>). IgAN accounted for close to 50% of cases at age 19 to 39 years. The prevalence of IgAN was about 40% in the ages 40 to 59 years. However, in patients older than 60 years, the prevalence of IgAN was < 20%, and the prevalence of FSGS and MN accounted for nearly 40%. The proportion of patients with MCD was the highest in patients aged 19 to 39 years.

3.3. Differences in pathological diagnoses according to the clinical syndrome at the time of kidney biopsy

The distribution of clinical syndromes differed from the pathological diagnoses. NS was dominant in MN, MCD, LN, DN, and thrombotic microangiopathy. AUA was dominant in thin basement membrane disease. RI was dominant in FSGS, crescentic

GN, HT-N, and TID. Patients who showed IP were diagnosed with FSGS, amyloidosis, LN, and DN (Fig. 4 and Supplementary Table S2, <http://links.lww.com/MD/G962>).

Fig. 5A shows the yearly change in the frequency of the 4 major glomerular diseases that account for the largest proportion of primary glomerular disease. IgAN was the most common glomerular disease for the entire period, but it has decreased since 2013. Secondary glomerular diseases tended to be more frequent in 2019 than in 2013. The incidence of LN and HT-N did not vary significantly from year to year, but the prevalence of DN has been on the rise (Fig. 5B). Although TID and vascular disease differed slightly every year, no specific trend was found for the entire period (Fig. 5C).

3.4. Differences in pathological diagnoses according to comorbidities

Fig. 6 shows the distribution of the 5 most common pathological diagnoses according to comorbidities. The most common

Table 4
Clinical characteristics and laboratory findings of patients based on pathological diagnoses.

	Age (years)	Male (n, %)	eGFR (mL/min/1.73m ²)	BMI (kg/m ²)	MAP (mm Hg)	Total (n, %)
Primary glomerular disease						450 (71.3)
IgAN	44.8 ± 16.3	119 (53.8)	74.9 ± 39.8	24.3 ± 4.2	99.4 ± 15.0	221 (35.0)
FSGS	56.0 ± 17.8	70 (62.5)	64.7 ± 44.1	24.9 ± 4.4	101.4 ± 18.0	112 (17.7)
MN	59.4 ± 17.1	45 (73.8)	96.2 ± 43.9	25.2 ± 3.7	98.1 ± 14.9	61 (9.7)
MCD	45.2 ± 20.2	18 (56.2)	107.3 ± 51.0	26.1 ± 4.0	99.7 ± 13.1	32 (5.1)
Crescentic GN	62.9 ± 14.2	9 (64.3)	17.2 ± 23.4	24.5 ± 3.2	99.3 ± 17.7	14 (2.2)
MPGN	66.8 ± 12.5	4 (40.0)	65.0 ± 28.7	23.7 ± 3.3	109.2 ± 12.7	10 (1.6)
Secondary glomerular disease						107 (16.9)
DN	55.7 ± 12.6	28 (73.7)	38.5 ± 24.2	25.0 ± 4.0	106.7 ± 17.3	38 (6.0)
LN	42.4 ± 15.1	2 (7.4)	100.2 ± 55.3	22.9 ± 3.0	98.1 ± 17.2	27 (4.3)
HT-N	54.6 ± 17.5	14 (56.0)	38.9 ± 32.3	27.6 ± 4.6	119.7 ± 24.7	25 (4.0)
Amyloidosis	62.9 ± 7.6	3 (42.9)	67.4 ± 33.9	23.0 ± 1.2	95.1 ± 19.8	7 (1.1)
MIDD	63.5 ± 11.0	4 (66.7)	40.0 ± 45.4	20.8 ± 3.5	100.3 ± 21.2	6 (0.9)
HSP	49.0 ± 23.0	2 (50.0)	83.3 ± 50.4	23.1 ± 2.6	89.6 ± 2.0	4 (0.6)
Tubulointerstitial disease						34 (5.4)
ATIN	58.6 ± 16.6	12 (80.0)	24.8 ± 18.8	22.6 ± 3.7	98.8 ± 21.1	15 (2.4)
CTIN	59.9 ± 17.4	7 (36.8)	36.5 ± 29.7	22.7 ± 3.1	92.3 ± 11.9	19 (3.0)
Vascular disease: TMA	66.4 ± 15.5	3 (60.0)	42.5 ± 18.1	23.7 ± 4.6	92.8 ± 6.0	5 (0.8)
Hereditary renal disease						5 (0.8)
TBMD	29.2 ± 19.2	2 (50.0)	113.1 ± 36.9	22.8 ± 3.5	89.5 ± 6.4	4 (0.6)
Alport syndrome	58.0 ± 0.0	0 (0.0)	41.3 ± 0.0	22.5 ± 0.0	110.0 ± 0.0	1 (0.2)
ESRD	49.2 ± 23.1	2 (40.0)	12.2 ± 6.9	22.7 ± 2.4	103.0 ± 12.8	5 (0.8)
Other/miscellaneous	50.2 ± 21.5	18 (72.0)	64.5 ± 43.9	25.1 ± 4.9	105.8 ± 12.0	25 (4.0)

Values are presented as the mean ± SD or number (%). The bold values are the category of pathological diagnosis.
 ATIN = acute tubulointerstitial nephritis, BMI = body mass index, CTIN = chronic tubulointerstitial nephritis, DN = diabetic nephropathy, eGFR = estimated glomerular filtration rate, ESRD = end-stage renal disease, FSGS = focal segmental glomerulosclerosis, GN = glomerulonephritis, HSP = Henoch-Schönlein purpura, HT-N = hypertensive nephropathy, IgAN = IgA nephropathy, LN = lupus nephritis, MAP = mean arterial pressure, MCD = minimal change disease, MIDD = monoclonal immunoglobulin deposition disease, MN = membranous nephropathy, MPGN = membranoproliferative GN, TBMD = thin basement membrane disease, TMA = thrombotic microangiopathy.

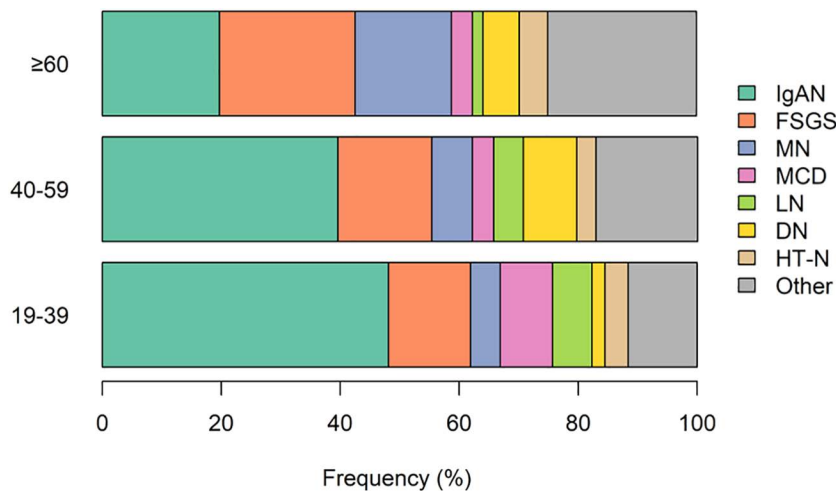


Figure 3. The distribution of glomerular diseases according to age. DN = diabetic nephropathy, FSGS = focal segmental glomerulosclerosis, HT-N = hypertensive nephropathy, IgAN = immunoglobulin A nephropathy, LN = lupus nephritis, MCD = minimal change disease, MN = membranous nephropathy.

pathological diagnosis in patients with DM was DN (33%), followed by IgAN (16.5%), FSGS (15.7%), and MN (9.6%) (Fig. 6A). Kim et al^[15] reported that DN was 28.1% and IgAN was 23.1% in patients with DM, too (Supplementary Table S3, <http://links.lww.com/MD/G962>). The most common pathological diagnosis in patients with HT was IgAN (33.4%), followed by FSGS (20.1%). HT-N ranked fourth (8%) in those patients (Fig. 6B). IgAN was the most common and HT-N ranked the fourth (4.6%) in patients with HT in Kim et al's^[15] report too (Supplementary Table S4, <http://links.lww.com/MD/G962>). In patients with viral hepatitis or malignancy, IgAN was also the most common glomerular disease, accounting for 22.7% and 32.3% of patients, respectively (Fig. 6C and 6D) (Supplementary Tables S5 and S6, <http://links.lww.com/MD/G962>).

3.5. Comparison of pathological distributions between Korean studies

Primary glomerular disease was more common than secondary one in all Korean studies (Table 5). IgAN was the most common primary glomerular disease. The second common primary glomerular disease was different; MCD in Chang et al's^[12] and Yim et al's^[14] studies; MN in Shin et al's^[13] and Kim et al's^[15] studies; FSGS in our study. The most common secondary glomerular disease was DN in our study and LN in the others. The most common clinical syndrome was AUA in Yim et al's^[14] and Shin et al's^[13] studies and RI in our study (Supplementary Table S7, <http://links.lww.com/MD/G962>).

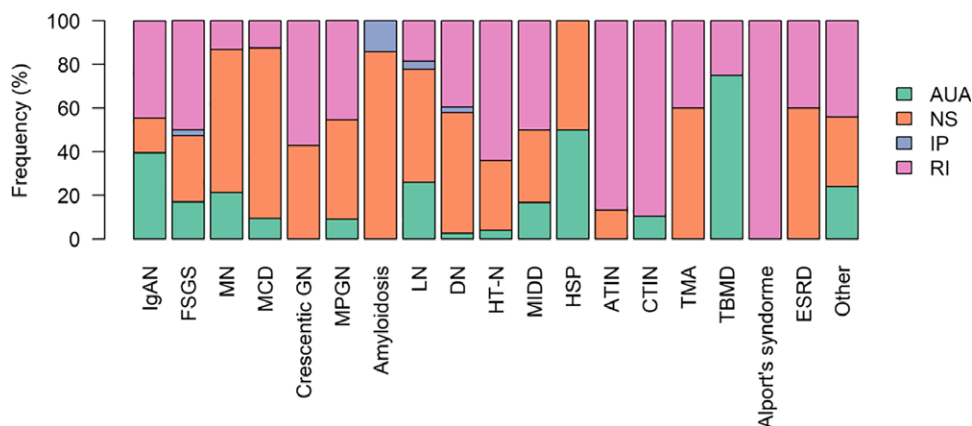


Figure 4. The distribution of clinical syndromes according to pathological diagnoses. ATIN, acute tubulointerstitial nephritis, AUA = asymptomatic urinary abnormality, CTIN = chronic tubulointerstitial nephritis, DN = diabetic nephropathy, ESRD = end-stage renal disease, FSGS = focal segmental glomerulosclerosis, GN = glomerulonephritis, HSP = Henoch-Schönlein purpura, HT-N = hypertensive nephropathy, IgAN = immunoglobulin A nephropathy, IP = isolated proteinuria, LN = lupus nephritis, MCD = minimal change disease, MIDD = monoclonal immunoglobulin deposition disease, MN = membranous nephropathy, MPGN = membranoproliferative GN, NS = nephrotic syndrome, RI = renal insufficiency, TBMD = thin basement membrane disease, TMA = thrombotic microangiopathy.

4. Discussion

This is the first time the results of kidney biopsies conducted in the Gyeongnam province of South Korea have been analyzed. We examined data from 2013 to 2019 because the electronic medical recording system was introduced in this center in 2013, and large omissions were found in the paper medical records from before 2013.

The indications for a kidney biopsy are based on clinical syndromes. Kidney biopsy is usually considered in NS, acute nephritic syndrome, and unexplained AKI and sometimes in isolated glomerular hematuria and IP.^[21] The number of cases of kidney biopsy in patients with IP has been increasing. Among the 6 patients with IP, 3 had FSGS, 1 had early DN, and other pathological findings were LN and amyloidosis. According to a study by Hladunewich et al,^[22] nearly 40% of patients with idiopathic MGN had non-nephrotic range proteinuria throughout the observation period, and their long-term prognosis, when treated, was more favorable than those with high-grade proteinuria. Christopher-Stine et al^[23] reported that significant renal involvement was found on kidney biopsies from patients with systemic lupus erythematosus (SLE) and low-level proteinuria (<1g/day). Hama et al^[24] analyzed pediatric patients and found a high diagnosis rate of FSGS and IgAN, especially in the group with uPCR of 0.5 mg/mg or higher. They suggested that the indication for kidney biopsy in pediatric patients with asymptomatic, constant IP is uPCR ≥ 0.5 g/g. Clinically important kidney disease can be diagnosed through a kidney biopsy in a patient with non-nephrotic range proteinuria, so that should be considered when deciding whether to perform a kidney biopsy. Yim et al^[14] reported that 62.5% of kidney biopsies returned findings of AUA, but AUA was found in only 23.1% of patients in our study. Perhaps we performed kidney biopsies more conservatively than in the earlier study.

The prevalence of T1D is often underestimated. In acute renal failure of unknown cause, acute interstitial nephritis is diagnosed through renal biopsy in fewer than 15% of cases.^[25] This can be inferred to be lower than the actual incidence of this disease. Clinicians sometimes diagnose acute tubulointerstitial nephritis (ATIN) in patients with elevated serum creatinine levels by empirically discontinuing the drug suspected to be the cause without ordering a kidney biopsy. In our entire kidney biopsy cohort, T1D was found in 6.5% of patients, and ATIN was found in 7.5% of the 200 patients with AKI. The most common causative agent of ATIN was vancomycin in our cohort (data not shown). Vancomycin-induced ATIN is known to occur

when concomitant administration with other nephrotoxic drugs or high doses are used.^[26]

The most common primary glomerular disease in our center was IgAN, which is the most common primary glomerular disease in Europe and Asia, including other previously reported cohorts from South Korea.^[7,12-14] In our study, FSGS was the second-most common disease (15.7%), and among those FSGS patients, only 20% had nephrotic range proteinuria. This suggests that secondary FSGS might have been included in our patients. In fact, IP is not a typical kidney biopsy indication, as mentioned above, but in our study, these patients were diagnosed with FSGS and early DN.

Control of blood pressure in renal disease is important.^[27] The KDIGO blood pressure guideline suggests that patients with CKD should be treated to a target SBP of < 120 mm Hg.^[28]

The mean blood pressure at the time of kidney biopsy showed a tendency to increase in the trend test according to the year. However, it is difficult to use our data to explain the effect of blood pressure on a patient's kidney disease because we collected only a single measurement of blood pressure when the patient was hospitalized for a kidney biopsy. It is necessary to follow-up and control HT after the kidney biopsy.

At the time of kidney biopsy, 115 patients had DM, but only 38 of them (33.0%) were diagnosed with DN. DN was the most common pathological diagnosis in DM patients, but the remaining 77 patients (67%) were diagnosed with other glomerular diseases not related to diabetes, predominantly IgAN, FSGS, and MN in that order. In another cohort study in South Korea, DN was the most common diagnosis in DM patients, followed by IgAN and MN. FSGS was the fourth-most common disease.^[14,15]

Even if DM or HT is present, another primary glomerular disease could be present. So, patients with DM or HT should be considered for kidney biopsy depending on the duration of their disease, other organ invasion, and their clinical presentation. HT was the most common comorbidity in our study, but only a small number of patients had HT-N confirmed in their kidney biopsy. Secondary hypertension can be induced by glomerular inflammation, as in nephritic syndrome.^[29]

Because the most common secondary glomerular disease was DN, we need to discuss the indications for performing kidney biopsies in DM patients. DN might have had the highest frequency among secondary glomerular diseases in our study because more biopsies were performed in patients with a high probability of DN. A kidney biopsy is not essential for diagnosing DN, which can also be diagnosed clinically.^[30] Although

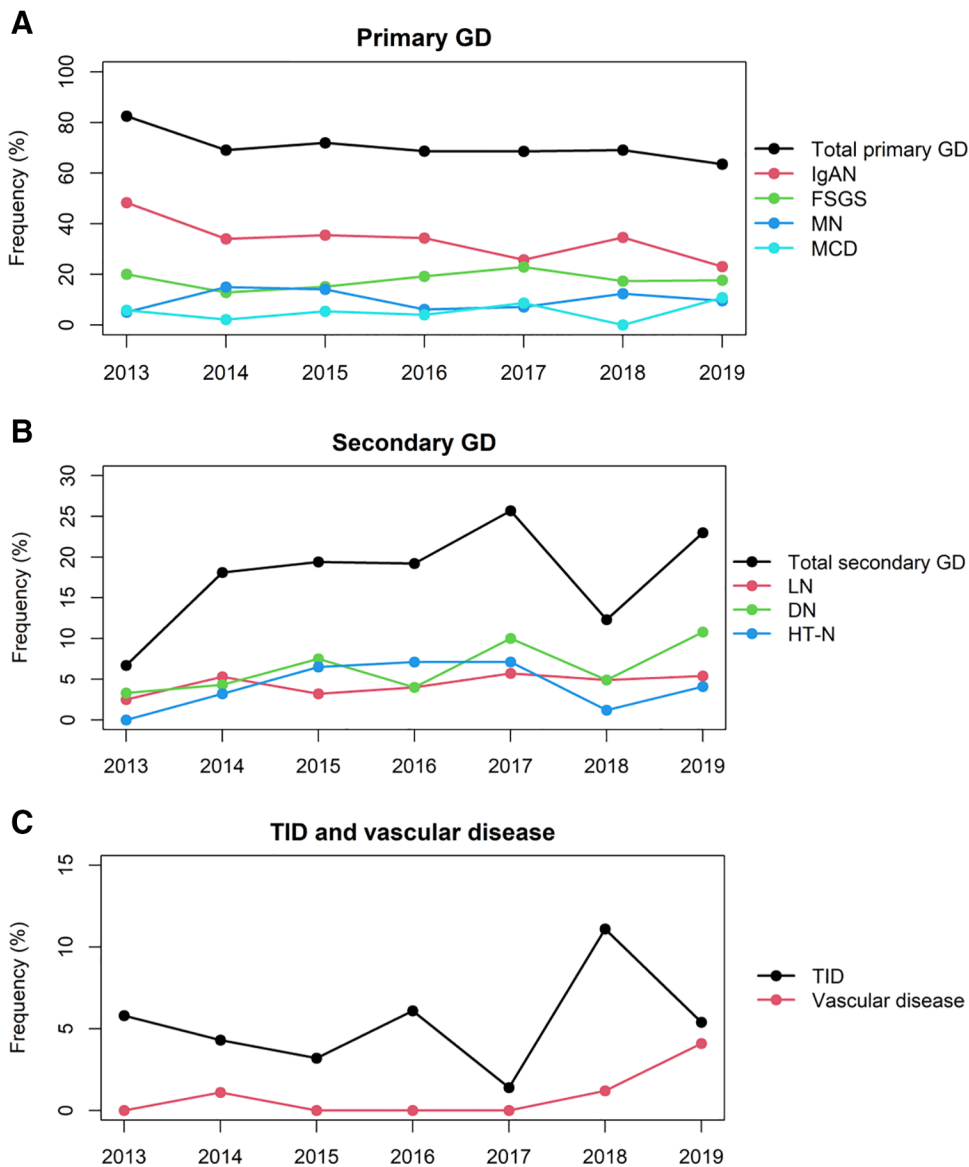


Figure 5. Annual prevalence of various pathological findings and temporal trends in disease frequency. (A) The annual prevalence of primary glomerular disease. (B) The annual prevalence of secondary glomerular disease. (C) The annual prevalence of tubulointerstitial disease and vascular disease. DN = diabetic nephropathy, FSGS = focal segmental glomerulosclerosis, GD = glomerular disease, HT-N = hypertensive nephropathy, IgAN = immunoglobulin A nephropathy, LN = lupus nephritis, MCD = minimal change disease, MIDD = monoclonal immunoglobulin deposition disease, MN = membranous nephropathy, TID = tubulointerstitial disease, TMA = thrombotic microangiopathy.

controversy remains about the most appropriate timing for kidney biopsy in type 2 DM patients, a 3-step approach considering diabetic retinopathy, DM duration, and hematuria has recently been proposed as potentially a useful tool.^[31]

LN was the most common secondary glomerular disease in Brazil, the Czech Republic, Spain, Australia, Hong Kong, China, and South Korea.^[11,13,32-36] But in our study, LN was the second-most common secondary glomerular disease, possibly because we performed more kidney biopsies in diabetic patients than lupus patients, which could itself reflect that our province contains fewer lupus patients than diabetic patients. According to a recent report by Bae et al,^[37] the incidence of SLE in Gyeongnam province was the lowest in South Korea during the survey period (2005–2015).

Glomerular injury can occur by means of an immune reaction to the hepatitis virus. The most common glomerular pathologic presentation in patients with hepatitis B is MN, and MPGN is the most common finding in hepatitis C patients.^[38] However,

the prevalence of IgAN is higher than that of other glomerular diseases in Asia, where viral hepatitis is endemic.^[39,40] In a recent Korean cohort study, IgAN was the most common diagnosis in patients with hepatitis B surface antigen, and the same result was found in patients with hepatitis C.^[41] Gyeongnam province shows a high prevalence of hepatitis B and C.^[41,42] In our study, IgAN was the most common diagnosis in patients with hepatitis B or C, although we did not separately analyze hepatitis B and C due to the small number of patients with viral hepatitis.

This study has certain limitations. Clinical syndromes with mild symptoms could be missed because we analyzed only the pathological diagnoses of patients who underwent a kidney biopsy. We had no data for patients who were clinically diagnosed without a kidney biopsy. Furthermore, this study might not fully represent all the patients in this province even though our center is the only tertiary hospital in this area because it is now easier to get to a large hospital in another province. Also, we need to consider the misclassification bias because we

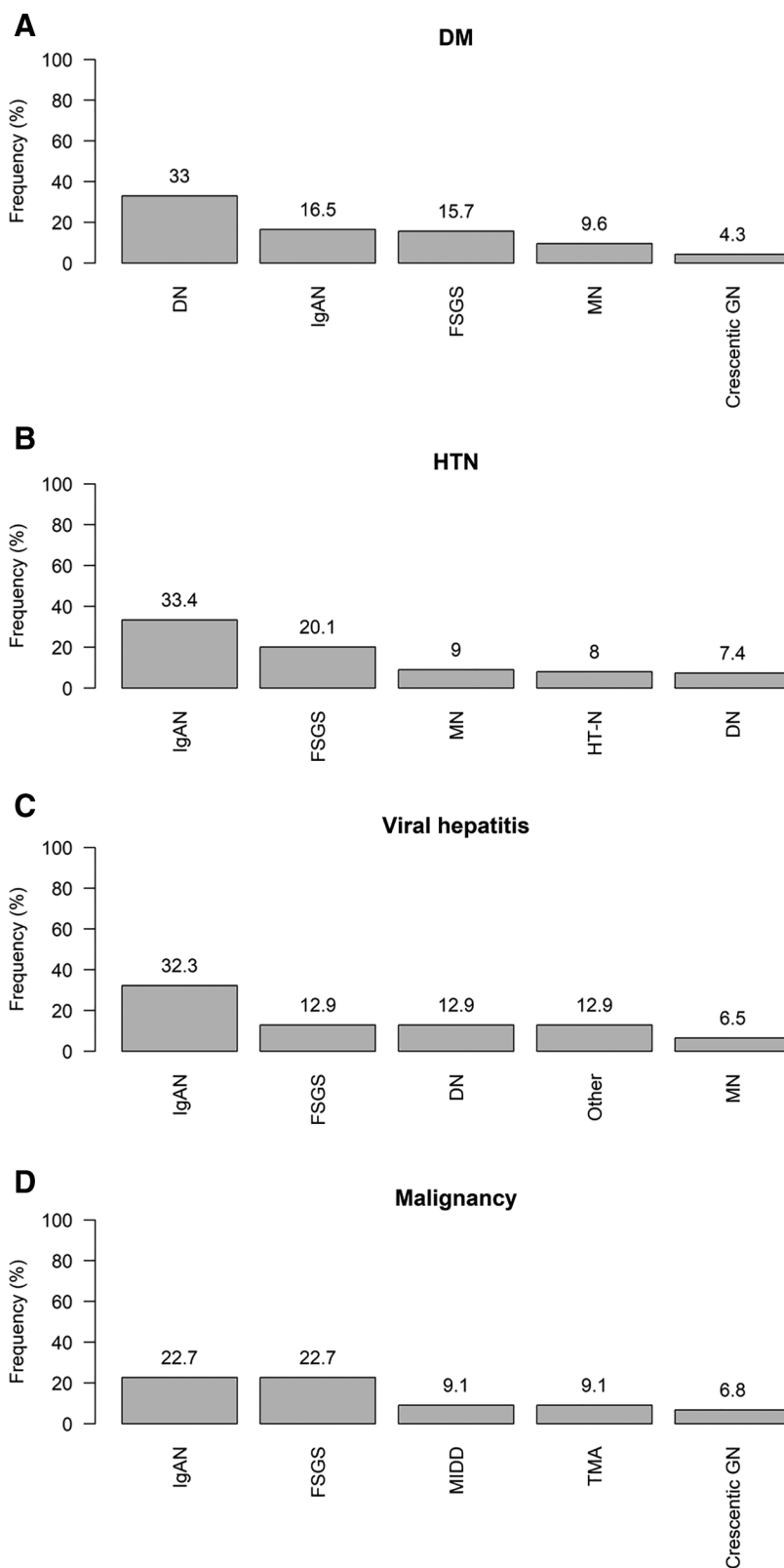


Figure 6. The distribution of pathological diagnoses according to comorbidities: (A) diabetes mellitus, (B) hypertension, (C) viral hepatitis, and (D) malignancy. DN = diabetic nephropathy, FSGS = focal segmental glomerulosclerosis, GN = glomerulonephritis, HT-N = hypertensive nephropathy, HTN = hypertension, IgAN = immunoglobulin A nephropathy, MN = membranous nephropathy.

retrospectively collected the information of patients from the recorded medical history.

In conclusion, this study has described the demographic characteristics and trends of patients diagnosed with kidney

disease through kidney biopsies in Gyeongnam province in South Korea. The most common clinical syndrome was RI. IgAN and DN were the most common primary and secondary glomerular diseases, respectively. Our data can be a useful

Table 5
Comparison of pathologic distribution in Korean studies.

Diagnosis	Chang et al ^[12]	Shin et al ^[13]	Yim et al ^[14]	Kim et al ^[15]	Present study
Study duration	1987–2006	1992–2011	2001–2013	1979–2018	2013–2019
Region	Seoul	Pusan	Gyeongpook/Daegu	South Korea	Gyeongnam
Number of centers	1	1	1	18	1
Total population	10,212, 056	3,550,963	2,699,440/2,501,588	51,826,059	3,314,183
Total biopsy	1818 (100.0)	818 (100.0)	1924 (100.0)	21,426	631 (100.0)
Primary GD	1346 (74.0)	664 (81.2)	1252 (65.1)	14,487 (67.6)	450 (71.4)
IgAN	514 (28.3)	211 (25.8)	719 (37.4)	7586 (34.2)	221 (35.0)
MsPGN	—	224 (27.4)	—	—	—
MCD	282 (15.5)	28 (3.4)	170 (8.8)	2028 (9.1)	32 (5.1)
MN	223 (12.3)	62 (7.6)	147 (7.6)	2035 (9.2)	61 (9.7)
FSGS	101 (5.6)	27 (3.3)	130 (6.8)	1698 (7.7)	112 (17.7)
MPGN	72 (4.0)	53 (6.5)	20 (1.0)	585 (2.6)	10 (1.6)
Others	154 (8.5)	50 (6.2)	22 (1.1)	145 (0.7)	NR
Crescentic GN	NR	9 (1.1)	44 (2.3)	410 (1.9)	14 (2.2)
Secondary GD	215 (11.8)	46 (5.6)	198 (10.3)	3535 (16.5)	107 (16.9)
LN	159 (8.7)	23 (2.8)	88 (4.6)	1398 (6.3)	27 (4.3)
DN	36 (2.0)	1 (0.1)	25 (1.3)	887 (4.0)	38 (6.0)
HSP	18 (1.0)	5 (0.6)	28 (2.0)	290 (1.3)	4 (0.6)
ANCA-AV	NR	2 (0.2)	11 (0.6)	66 (0.3)	NR
PSGN	NR	5 (0.6)	NR	177 (0.8)	NR
Amyloidosis	NR	5 (0.6)	NR	196 (0.9)	7 (1.1)
MIDD	NR	2 (0.2)	NR	35 (0.2)	6 (0.9)
TMA	NR	2 (0.2)	NR	90 (0.4)	5 (0.8)
HT-N	NR	1 (0.1)	NR	372 (1.7)	25 (4.0)
Others	2 (0.1)	0 (0.0)	36 (1.9)	24 (0.1)	NR
Hereditary GD	NR	4 (0.5)	383 (19.9)	748 (3.4)	5 (0.8)
TBMD	—	4 (0.5)	377 (19.6)	690 (3.1)	4 (0.6)
Alport syndrome	—	NR	6 (0.3)	58 (0.3)	1 (0.2)
Normal or minor change	141 (7.8)	99 (11.2)	84 (4.4)	546 (2.5)/53 (0.2)	15 (2.4)
Others	116 (6.4)	1 (0.1)	NR	228 (1.0)	10 (1.6)
TIN	NR	11 (1.3)	7 (0.4)	1382 (6.4)	34 (5.4)
Myeloma kidney	—	—	—	63 (0.3)	—

Values were presented as number (%). The bold values are the category of pathological diagnosis.

ANCA-AV = ANCA-associated vasculitis, DN = diabetic nephropathy, FSGS = focal segmental glomerulosclerosis, GD = glomerular disease, HSP = Henoch-Schönlein purpura, HT-N = hypertensive nephropathy, IgAN = IgA nephropathy, LN = lupus nephritis, MCD = minimal change disease, MIDD = monoclonal immunoglobulin deposition disease, MN = membranous nephropathy, MPGN = membranoproliferative glomerulonephritis, MsPGN = mesangial proliferative glomerulonephritis, NR = not reported, PSGN = poststreptococcal glomerulonephritis, TBMD = thin basement membrane disease, TIN = tubulointerstitial nephritis, TMA = thrombotic microangiopathy.

reference for diagnosing kidney disease and understanding the patients in our province. Patients diagnosed with rare or incurable diseases can receive economic and social support from the national insurance system. Therefore, this study can be used as basic data to predict changes in the characteristics of these diseases, which is expected to provide important information for establishing hospitals and national insurance policies.

Author contributions

Conceptualization: HJK, SHL.
 Formal analysis: SHL, MJK, HJK.
 Visualization: MJK, SHJ.
 Writing-original draft: SHL, SHJ, HJK.
 Writing-review/editing : SHC, HNJ, JSL, HJK.
 The relevant clinical details are presented in this study.

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