ORIGINAL ARTICLE

Correlation between Clinical Manifestations of Glomerular Disease and Renal Pathologies in an Urban Thai Population

Natthanan Krajangjaeng, MD[1], Tanun Ngamvichchukorn, MD[1]

[1] Department of Medicine, Faculty of Medicine Vajira Hospital, Navamindradhiraj University, Bangkok, Thailand

Background: Glomerular disease is a common cause of end-stage renal disease. The diagnosis of glomerular disease requires evaluation and confirmation by renal biopsy, which is crucial for accurate disease classification, prognosis, and management. Although numerous population-based epidemiological studies have been conducted globally, variations in clinicopathological correlations persist.

Objective: The present study aimed to investigate the relationship between the clinical manifestations of glomerular disease and histopathological diagnoses in urban Thai patients with glomerular disease.

Materials and Methods: This retrospective study included patients with clinical manifestations suggestive of glomerular disease who underwent native renal biopsy at Vajira Hospital, Bangkok, Thailand, between 2019 and 2022. Data, including age, gender, underlying disease, laboratory data, clinical symptoms, and pathological diagnoses, were obtained.

Results: A total of 401 patients with a mean age of 44.40±15.20 years were included in the present study. Of the 401 patients, 242 were females (60.3%), and 159 were males (39.7%). The most common clinical manifestation was asymptomatic proteinuria (42.4%), followed by nephrotic syndrome (36.2%), nephritic syndrome (9%), rapidly progressive glomerulonephritis (5.7%), asymptomatic hematuria (4%), and chronic glomerulonephritis (2.7%). Lupus nephritis (LN) (23.7%), IgA nephropathy (21.9%), and diabetic nephropathy (DN) (21.9%) were the most common histopathological diagnoses. Asymptomatic proteinuria was most associated with DN and IgA nephropathy, whereas nephrotic syndrome was frequently linked to LN and DN.

Conclusion: The predominant clinical manifestation was asymptomatic proteinuria, and the main pathological finding was LN. The present study provides valuable insights into the correlation between the clinical manifestations of glomerular disease and renal pathology and sheds light on the diverse clinical manifestations and underlying pathological diagnoses in patients with glomerular disease.

Keywords: Glomerular disease; Renal biopsy; Renal pathology

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Glomerular diseases are characterized by abnormalities in the glomeruli of the kidneys. These diseases are frequently encountered in modern clinical practice and include IgA nephropathy (IgAN), IgM nephropathy (IgMN), minimal change disease (MCD), membranous nephropathy (MN), membranoproliferative glomerulonephritis (MPGN), focal segmental glomerulosclerosis (FSGS), lupus nephritis (LN), diabetic nephropathy (DN), antineutrophil cytoplasmic antibody-associated vasculitis, antiglomerular basement membrane antibody glomerulonephritis, and postinfectious glomerulonephritis[1]. Glomerular diseases are classified into two types: primary glomerular disease, where the pathology originates solely in the glomeruli, and secondary glomerular disease, which arises due to underlying systemic conditions. Autoimmune diseases, such as systemic lupus erythematosus (SLE), infections, such as hepatitis B, hepatitis C, and HIV, cancers, and certain medications are common causes of secondary glomerular disease[1]. Inappropriate diagnosis and treatment can increase the risk of chronic kidney disease and end-stage renal disease, necessitating renal replacement therapy, which subsequently increases mortality and disability rates[2]. Diagnosis of glomerular disease requires a renal biopsy to assess the pathology and to guide treatment and prognosis[1]. Each patient has specific indications for renal biopsy based on clinical manifestations.

A prospective study in Japan showed that chronic

Correspondence to:

Ngamvichchukorn T.

Division of Nephrology, Department of Medicine, Faculty of Medicine Vajira Hospital, Navamindradhiraj University, Bangkok 10300, Thailand.

Phone: +66-2-2443482

Email: tanun@nmu.ac.th

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nephritic syndrome was the most common clinical manifestation of glomerular disease[3]. In contrast, a study in Poland showed that nephrotic-range proteinuria was the most common clinical manifestation, with MN being the most frequently observed disease in this group[4]. Similarly, a retrospective study in Northeast China showed that nephrotic syndrome is the most prevalent clinical manifestation, with MN being the most commonly associated disease[5]. A retrospective study in Thailand, which included 3,555 renal biopsy patients, reported that nephrotic and nephritic-nephrotic syndrome were the most common clinical manifestations. IgMN was the most frequent glomerular disease associated with nephrotic syndrome in this population, which differed from other countries where MCD and MN were more common[6].

Clinical manifestations and underlying glomerular diseases vary across regions and populations. The diverse clinical symptoms associated with glomerular disease often correspond to distinct pathological findings on renal biopsy, which may be influenced by various risk factors. Furthermore, each glomerular disease has distinct long-term implications, particularly in terms of the risk of end-stage renal disease (ESRD), mortality rates, and years of life lost (YLL). A retrospective observational cohort study assessing mortality, ESRD rates, and YLL in Thai patients with biopsy-confirmed glomerular disease revealed that paraprotein-related kidney disease had the highest mortality rate, whereas diabetic nephropathy had the highest ESRD rate. Although lupus nephritis (LN) did not have the highest mortality rate, it contributed to the greatest YLL (41% of all glomerular diseases) and was strongly associated with significant premature mortality before the age of 60[7]. These findings emphasize the critical role of accurate glomerular disease diagnosis in predicting long-term outcomes and YLL in Thailand.

Therefore, the present study aimed to investigate the relationship between the clinical manifestations of glomerular diseases and renal biopsy pathology in urban Thai patients. Additionally, this study aimed to compare renal pathology between patients with and without diabetes, those with low and normal complement 3 (C3) levels, and those with nephrotic and sub-nephrotic-range proteinuria.

Materials and Methods

This retrospective descriptive study included patients aged 15 years or older who presented with clinical syndromes consistent with glomerular disease and underwent renal biopsy at Vajira Hospital between January 1, 2019, and December 31, 2022. Patients were categorized into the following glomerular syndromes based on clinical and laboratory findings: Asymptomatic Hematuria, Asymptomatic Proteinuria, Nephritic Syndrome, Nephrotic Syndrome (NS), Rapidly Progressive Glomerulonephritis (RPGN), and Chronic Glomerulonephritis (CGN).

The present study received ethical approval from the Institutional Review Board of the Faculty of Medicine, Vajira Hospital, under Certificate of Approval No. 086/2566. Patients with indeterminate biopsy results or a history of kidney transplantation were excluded. In cases where multiple pathological findings were observed in a single renal biopsy sample, both diagnoses were reported.

The sample size was calculated to be 425. After accounting for a 10% incomplete data rate, 472 patients were required to be included in the present study. Data collected from medical records included demographics, comorbidities, laboratory results, clinical syndromes, and pathological diagnoses.

Qualitative data, such as sex and underlying diseases, were analyzed using frequency distributions, whereas quantitative data, such as age and creatinine levels, were presented as means, standard deviations, or medians, as appropriate. The association between renal biopsy findings and clinical manifestations was evaluated using Pearson's Chi-square test or the Fisher-Freeman-Halton exact test. All analyses were performed using IBM SPSS Statistics version 28.0, and a p-value less than 0.05 was considered statistically significant.

Results

Of the 472 patients who underwent renal biopsy and were initially enrolled in this study, 71 were excluded due to the following criteria: a history of kidney transplantation (n=48), inadequate renal tissue for definitive histopathological diagnosis (n=8), and clinical manifestations inconsistent with glomerular disease (n=15). Consequently, 401 patients were included in the final analysis.

Baseline characteristics, including demographic data, comorbid conditions, and laboratory findings for the overall cohort and each clinical presentation category, are detailed in Table 1. The mean age of the study population was 44.4±15.2 years, with a predominance of female patients (n=242, 60.3%). The most prevalent comorbidities were hypertension (56.9%), hyperlipidemia (32.4%), and diabetes mellitus (29.2%). Among the clinical syndromes, patients presenting with asymptomatic hematuria had the highest mean age (50.56±18.54 years), whereas those diagnosed with chronic glomerulonephritis (CGN) and nephritic syndrome were comparatively younger, with mean ages of 39.55±14.15 and 38.39±14.79 years, respectively. Diabetes mellitus was most frequently observed in patients with nephrotic syndrome (35.9%) and asymptomatic proteinuria (32.9%). In contrast, hypertension was more prevalent among patients with asymptomatic proteinuria (67.6%) and CGN (54.5%). The estimated glomerular filtration rate

Table 1. Baseline characteristics of the population classified by clinical presentations of glomerular disease

Biopsy (n, %)	Total (n=401)	Hematuria (n=16)	Proteinuria (n=170)	Nephritic syndrome (n=36)	Nephrotic syndrome (n=145)	RPGN (n=23)	CGN (n=11)	p-value
Age (mean ± SD)	44.40±15.20	50.56±18.54	46.77±14.32	38.39±14.79	43.37±15.05	40.83±17.52	39.55±14.15	0.003 a
Sex								0.028 b
Male	159 (39.7)	3 (18.8)	74 (43.5)	9 (25.0)	55 (37.9)	10 (43.5)	8 (72.7)	
Female	242 (60.3)	13 (81.3)	93 (56.5)	27 (75.0)	90 (62.1)	13 (56.5)	3 (27.3)	
DM	117 (29.2)	2 (12.5)	56 (32.9)	3 (8.3)	52 (35.9)	3 (13.0)	1 (9.1)	0.002 b
HT	228 (56.9)	7 (43.8)	115 (67.6)	16 (44.4)	75 (51.7)	9 (39.1)	6 (54.5)	0.008 b
DLP	130 (32.4)	7 (43.8)	66 (38.8)	4 (11.1)	46 (31.7)	5 (21.7)	2 (18.2)	0.017 b
CAD	14 (3.5)	-	7 (4.1)	-	5 (3.4)	1 (4.3)	1 (9.1)	0.605 c
CVA	19 (4.7)	1 (6.3)	13 (7.6)	-	5 (3.4)	-	-	0.268 c
SLE	95 (23.7)	6 (37.5)	34 (20.0)	9 (25.0)	37 (25.5)	8 (34.8)	1 (9.1)	0.290 b
HBV infection	18 (4.5)	-	7 (4.1)	-	8 (5.5)	2 (8.7)	1 (9.1)	0.637 c
HCV infection	15 (3.7)	-	9 (5.3)	-	4 (2.8)	-	2 (18.2)	0.300 c
HIV infection	13 (3.2)	-	10 (5.9)	-	2 (1.4)	-	1 (9.1)	0.452 c
BUN (mean ± SD)	28.53±18.57	24.19±14.07	26.93±15.11	28.15±13.84	26.62±17.61	50.52±32.99	36.64±24.46	<0.001 a
Cr (mean ± SD)	2.11±1.93	1.57±0.71	2.12±1.63	1.72±0.62	1.69±1.29	4.50±4.39	4.04±3.27	<0.001 a
eGFR (mean ± SD)	54.34±36.79	52.72±30.65	53.20±38.26	49.18±27.66	64.09±37.03	23.17±18.61	32.66±25.97	<0.001 a
Albumin (mean ± SD)	3.33±2.22	3.58±0.77	3.82±3.29	3.46±0.75	2.73±0.89	3.31±0.73	3.62±0.63	<0.001 a
UPCR (mean ± SD)	4.58±3.98	1.56±1.52	3.70±3.35	2.61±2.07	6.73±4.50	3.94±2.69	2.22±18.5	<0.001 a
Urine profile WBC >5	258 (64.3)	12 (75.0)	91 (53.5)	25 (69.4)	106 (73.1)	18 (78.3)	6 (54.5)	0.011 b
Urine profile RBC >5	241 (60.1)	15 (93.8)	79 (46.5)	32 (88.9)	87 (60.0)	19 (82.6)	9 (81.8)	<0.001 b

The p-value by [a] Kruskal-Wallis test, [b] Pearson Chi-square test, [c] Fisher-Freeman-Halton exact test, significant level at $p<0.05$

(eGFR) was highest in patients with nephrotic syndrome (64.09±37.03 ml/min/1.73 m²) and lowest in those with rapidly progressive glomerulonephritis (23.17±18.61 ml/min/1.73 m²). Furthermore, the urine protein-to-creatinine ratio (uPCR) was markedly elevated in patients with nephrotic syndrome (6.73±4.5 g/gCr) and lowest in those with asymptomatic hematuria (1.56±1.52 g/gCr).

Patients with tubulointerstitial disease had the highest mean age of 69.67±12.42 years, whereas those with thrombotic microangiopathy were the youngest (average age 21.67±9.87 years). Hypertension was most frequently observed in patients with DN (92%) and MPGN (80%). The estimated glomerular filtration rate was lowest in patients with acute tubular necrosis (mean 8.9±2.48 ml/min/1.73 m²) (Table 2).

The most common clinical manifestation was asymptomatic proteinuria (42.4%), followed by nephrotic syndrome (36.2%). The predominant pathological diagnosis was LN (23.7%), followed by IgAN (21.9%), DN (21.9%), and FSGS (12%).

Among patients presenting with asymptomatic hematuria, IgAN was the most prevalent pathological finding (43.8%), followed by LN (25%) and MPGN (18.8%). In patients with asymptomatic proteinuria, the most common diagnoses were DN (25.9%), IgAN (23.5%), FSGS (17.6%), and LN (17.6%). In cases of nephritic syndrome, IgAN was the predominant diagnosis (47.2%), followed by LN (25%). For patients presenting with nephrotic syndrome, LN was the most frequent diagnosis (29.7%), followed closely by DN (28.3%) and MN (11%). Among patients presenting with RPGN, LN (34.8%) and IgAN (21.7%) were the most common diagnoses, while ANCA-associated GN and MPGN were each observed in 8.7% of cases. For those diagnosed with CGN, the most frequent pathological findings were IgAN (54.5%), diffuse glomerulosclerosis (27.3%), and acute tubular necrosis (9.1%) (Table 3).

Pathological findings from renal biopsies stratified by diabetic and non-diabetic patients are presented in Table 4. The most prevalent pathological diagnosis among diabetic patients was diabetic nephropathy (DN), accounting for 74.4% of cases. In contrast, lupus nephritis (LN) was the most common finding among non-diabetic patients, observed in 32.7% of cases.

Diabetic patients predominantly presented with asymptomatic proteinuria (47.9%) and nephrotic syndrome (44.4%). In this cohort, DN was the most frequent pathological diagnosis in those presenting with asymptomatic proteinuria and nephrotic syndrome, comprising 76.8% and 78.8% of cases, respectively.

Among non-diabetic patients, asymptomatic proteinuria (40.3%) and nephrotic syndrome (32.5%) were the most common clinical presentations. For non-diabetic patients presenting with asymptomatic proteinuria, IgA nephropathy (IgAN) and LN were the leading pathological diagnoses, accounting for 28.1% and 26.3% of cases, respectively. In contrast, LN (46.7%) and membranous nephropathy (MN) (13%) were the most common diagnoses in non-diabetic patients with nephrotic syndrome (Table 4).

Statistical analysis revealed that patients with LN were significantly more likely to have low C3 levels (68.3%) than normal C3 levels (12.4%), $p<0.001$, whereas patients with normal C3 levels were more likely to be diagnosed with DN and IgAN (Table 5).

Patients with proteinuria in the sub-nephrotic range (uPCR 0.3 to 3.5 g/gCr) and nephrotic range (uPCR >3.5 g/gCr) were analyzed, comprising a total of 372 patients, as detailed in Table 6. Among patients with nephrotic-range proteinuria, the most common pathological diagnoses were diabetic nephropathy (DN) (35.2%) and lupus nephritis (LN) (23.5%). Conversely, patients with sub-nephrotic-range proteinuria were more frequently diagnosed with IgA nephropathy (IgAN) (34.7%) and LN (24.9%). Comparative analysis between the groups revealed that DN and membranous nephropathy (MN) were significantly more prevalent among patients with nephrotic-range proteinuria. In contrast, IgAN was significantly more common in patients with sub-nephrotic-range proteinuria.

Discussion

Patients with glomerular disease often present with diverse clinical manifestations, and the histopathological findings of renal biopsy vary according to the clinical manifestations. In the present study, most patients presented with asymptomatic proteinuria. This finding is consistent with that reported by Loreto et al. in Italy[8], who showed that urine abnormalities were commonly observed in patients who underwent renal biopsy. However, previous studies in Spain, Romania, and China have shown that most patients have nephrotic syndrome[5,9]. In contrast, a previous study conducted in Japan showed that most patients had chronic nephritic syndrome[3]. These differences in clinical manifestations may reflect varying indications for renal biopsy across countries.

In the present study, the most common histopathological diagnosis was LN, followed by IgAN and DN. This finding is consistent with that of a previous study in Thailand, which showed that LN was the most frequent diagnosis, followed by IgAN[10]. However, previous studies in Japan, Singapore, and Poland have shown that IgAN is the most common diagnosis[3,4,11]. A previous study in Thailand that included 3,555 patients who underwent renal biopsy showed that IgMN was the most common primary glomerular disease, whereas LN was the most frequent secondary glomerular disease[6]. These findings indicate that LN was the most

Table 2. Baseline characteristics of the population classified by renal biopsy pathology

Biopsy (n, %)	ATN (n=4)	Diffuse glomerulosclerosis (n=11)	DN (n=88)	FSGS (n=48)	IgA nephropathy (n=88)	LN (n=95)	MCD (n=27)	MN (n=17)	MPGN (n=10)	TMA (n=3)	Tubulointerstitial disease (n=3)
Age (mean ± SD)	47.75±18.25	43.27±15.70	53.03±12.67	48.25±15.80	43.85±13.45	35.18±11.95	42.22±15.05	50.12±19.92	47.30±17.31	21.67±9.87	69.67±12.42
Sex											
Male	1 (25.0)	9 (81.8)	50 (56.8)	23 (47.9)	41 (46.6)	10 (10.5)	12 (44.4)	8 (47.1)	3 (30.0)	1 (33.3)	-
Female	3 (75.0)	2 (18.2)	38 (43.2)	25 (52.1)	47 (53.4)	85 (89.5)	15 (55.6)	9 (52.9)	7 (70.0)	2 (66.7)	3 (100.0)
DM	1 (25.0)	3 (27.3)	87 (98.9)	9 (18.8)	15 (17.0)	2 (2.1)	3 (11.5)	5 (29.4)	3 (30.0)	-	2 (66.7)
HT	1 (25.0)	7 (63.6)	81 (92.0)	34 (70.8)	59 (67.0)	18 (18.9)	13 (48.1)	9 (52.9)	8 (80.0)	-	2 (66.7)
DLP	1 (25.0)	4 (36.4)	54 (61.4)	18 (37.5)	29 (33.0)	9 (9.5)	9 (34.6)	6 (35.3)	3 (30.0)	-	2 (66.7)
CAD	-	-	10 (11.4)	1 (2.1)	3 (3.4)	1 (1.1)	-	1 (5.9)	1 (10.0)	-	-
CVA	-	1 (9.1)	7 (8.0)	4 (8.3)	2 (2.3)	1 (1.1)	1 (3.8)	3 (17.6)	-	1 (33.3)	-
SLE	-	-	1 (1.1)	2 (4.2)	-	88 (92.6)	1 (3.8)	--	2 (20.0	1(33.3)	-
HBV infection	1 (25.0)	2 (22.2)	8 (10.0)	2 (6.3)	2 (2.8)	1 (1.3)	-	2 (12.5)	1 (12.5)	-	-
HCV infection	1 (25.0)	1 (11.1)	7 (9.1)	-	3 (4.2)	1 (1.3)	2 (9.1)	1 (6.7)	1 (14.3)	-	-
HIV infection	3 (75.0)	1 (11.1)	2 (2.5)	1 (3.4)	3 (4.2)	-	1 (5.3)	1 (6.7)	-	-	1 (33.3)
BUN (mean ± SD)	34.25±11.53	45.27±17.12	32.20±15.55	26.56±14.39	28.13±15.49	25.96±20.68	17.48±14.35	16.31±6.98	31.30±26.36	72.33±66.43	29.67±7.77
Cr (mean ± SD)	6.16±2.36	5.54±2.56	2.60±1.62	1.81±0.96	2.14±1.32	1.37±1.48	1.34±1.37	1.32±0.87	2.02±1.16	7.95±11.84	3.82±0.71
eGFR (mean ± SD)	8.90±2.48	14.45±9.09	36.17±25.24	52.64±35.26	44.61±25.32	79.80±38.03	81.42±40.30	71.89±38.57	44.07±27.94	66.47±80.63	11.53±1.62
Albumin (mean ± SD)	3.43±0.95	3.20±0.88	2.93±0.90	4.65±5.95	3.71±0.72	3.00±0.74	3.08±1.23	2.51±0.98	3.84±0.53	3.53±0.72	3.77±0.81
UPCR (mean ± SD)	3.49±1.71	4.26±2.89	7.14±4.58	3.31±2.40	2.97±3.23	3.90±3.25	6.11±5.36	7.88±6.60	3.11±2.48	2.53±2.16	3.95±1.71
Urine profile WBC >5	3 (75.0)	9 (81.8)	65 (77.4)	24 (53.3)	51 (63.0)	66 (73.3)	11 (50.0)	13 (81.3)	7 (70.0)	2 (66.7)	2 (66.7)
Urine profile RBC >5	2 (50.0)	7 (63.6)	51 (60.7)	19 (42.2)	58 (71.6)	66 (74.2)	9 (40.9)	9 (56.3)	8 (80.0)	2 (66.7)	1 (33.3)

Table 3. Renal biopsy pathology classified by clinical presentations of glomerular disease

Biopsy (n, %)	Total (n=401)	Hematuria (n=16)	Proteinuria (n=170)	Nephritic syndrome (n=36)	Nephrotic syndrome (n=145)	RPGN (n=23)	CGN (n=11)	p-value
ANCA-related GN	2 (0.5)	-	-	-	-	2 (8.7)	-	0.012 [b]
ATN	4 (1.0)	-	2 (1.2)	-	-	1 (4.3)	1 (9.1)	0.057 [b]
Diffuse glomerulosclerosis	11 (2.7)	-	6 (3.5)	-	1 (0.7)	1 (4.3)	3 (27.3)	0.005 [b]
DN	88 (21.9)	-	44 (25.9)	1 (2.8)	41 (28.3)	1 (4.3)	1 (9.1)	<0.001 [a]
FSGS	48 (12.0)	-	30 (17.6)	3 (8.3)	14 (9.7)	1 (4.3)	-	0.080 [b]
HIVICK	2 (0.5)	-	1 (0.6)	-	1 (0.7)	-	-	1.000 [b]
IgA nephropathy	88 (21.9)	7 (43.8)	40 (23.5)	17 (47.2)	13 (9.0)	5 (21.7)	6 (54.5)	<0.001 [a]
LN	95 (23.7)	4 (25.0)	30 (17.6)	9 (25.0)	43 (29.7)	8 (34.8)	1 (9.1)	0.101 [a]
MCD	27 (6.7)	-	13 (7.6)	-	14 (9.7)	-	-	0.215 [b]
MN	17 (4.2)	-	1 (0.6)	-	16 (11.0)	-	-	0.001 [b]
MPGN	10 (2.5)	3 (18.8)	1 (0.6)	1 (2.8)	2 (1.4)	2 (8.7)	1 (9.1)	0.001 [b]
PIGN	4 (1.0)	-	-	3 (8.3)	-	1 (4.3)	-	0.003 [b]
Renal amyloidosis	9 (2.2)	-	3 (1.8)	-	6 (4.1)	-	-	0.688 [b]
TMA	3 (0.7)	-	1 (0.6)	1 (2.8)	-	1 (4.3)	-	0.126 [b]
Tubulointerstitial disease	3 (0.7)	1 (6.3)	1 (0.6)	-	-	1 (4.3)	-	0.050 [b]
Other	12 (3.0)	1 (6.3)	7 (4.1)	2 (5.6)	1 (0.7)	1 (4.3)	-	0.158 [b]

The p-value by [a] Pearson Chi-square test; [b] Fisher-Freeman-Halton exact test; significant level at $p<0.05$

Table 4. Renal biopsy pathology classified by clinical presentations of glomerular disease in diabetic and non-diabetic patients

Biopsy (n, %)	DM (n = 117)						
	Hematuria (n = 2)	Proteinuria (n = 56)	Nephritic syndrome (n = 3)	Nephrotic syndrome (n = 52)	RPGN (n = 3)	CGN (n =1)	p-value
ANCA-related GN	-	-	-	-	-	-	n/a
ATN	-	1 (1.8)	-	-	-	-	1.000 [b]
Diffuse glomerulosclerosis	-	2 (3.6)	-	1 (1.9)	-	-	1.000 [b]
DN	-	43 (76.8)	1 (33.3)	41 (78.8)	1 (33.3)	1 (100.0)	0.027 [b]
FSGS	-	4 (7.1)	-	5 (9.6)	-	-	0.874 [b]
HIVICK	-		-	-	-	-	n/a
IgA nephropathy	-	8 (14.3)	1 (33.3)	5 (9.6)	1 (33.3)	-	0.413 [b]
LN	-		1 (33.3)	-	1 (33.3)	-	0.005 [b]
MCD	-	1 (1.8)	-	2 (3.8)	-	-	0.689 [b]
MN	-	1 (1.8)	-	4 (7.7)	-	-	0.461 [b]
MPGN	1 (50.0)	-	-	-	1 (33.3)	1 (100.0)	<0.001 [b]
PIGN	-	-	-	-	-	-	n/a
Renal amyloidosis	-	-	-	1 (1.9)	-	-	0.526 [b]
TMA	-	-	-	-	-	-	n/a
Tubulointerstitial disease	1 (50.0)	1 (1.8)	-	-	-	-	0.052 [b]
Other	-	3 (5.4)	-	-	-	-	0.396 [b]
Biopsy (n, %)	**Non-DM (n=283)**						
	Hematuria (n=14)	Proteinuria (n=114)	nephritic syndrome (n=33)	nephrotic syndrome (n=92)	RPGN (n=20)	CGN (n=10)	p-value
ANCA-related GN	-	-	-	-	2 (10.0)	-	0.009 [b]
ATN	-	1 (0.9)	-	-	1 (5.0)	1 (10.0)	0.056 [b]
Diffuse glomerulosclerosis		4 (3.5)			1 (5.0)	3 (30.0)	0.002 [b]
DN	-	1 (0.9)	-	-	-	-	1.000 [b]
FSGS		26 (22.8)	3 (9.1)	9 (9.8)	1 (5.0)		0.021 [b]
HIVICK	-	1 (0.9)	-	1 (1.1)	-	-	1.000 [b]
IgA nephropathy	7 (50.0)	32 (28.1)	16 (48.5)	8 (8.7)	4 (20.0)	6 (60.0)	<0.001 [a]
LN	4 (28.6)	30 (26.3)	8 (24.2)	43 (46.7)	7 (35.0)	1 (10.0)	0.016 [a]
MCD	-	12 (10.5)	-	11 (12.0)	-	-	0.121 [b]
MN	-	-	-	12 (13.0)	-	-	0.001 [b]
MPGN	2 (14.3)	1 (0.9)	1 (3.0)	2 (2.2)	1 (5.0)	-	0.086 [b]
PIGN	-	-	3 (9.1)	-	1 (5.0)	-	0.008 [b]
Renal amyloidosis	-	3 (2.6)	-	5 (5.4)	-		0.728 [b]
TMA	-	1 (0.9)	1 (3.0)	-	1 (5.0)	-	0.227 [b]
Tubulointerstitial disease	-	-	-	-	1 (5.0)	-	0.157 [b]
Other	1 (7.1)	4 (3.5)	2 (6.1)	1 (1.1)	1 (5.0)	-	0.341 [b]

The p-value by [a] Pearson Chi-square test; [b] Fisher-Freeman-Halton exact test, significant level at p<0.05

common diagnosis in patients with glomerular diseases in Thailand, potentially due to the increasing prevalence of SLE in the country.

When classifying histopathological findings according to clinical manifestations, DN was most commonly associated with asymptomatic proteinuria, whereas IgAN was most commonly associated with asymptomatic hematuria. Additionally, LN was most commonly associated with nephrotic syndrome. These findings are consistent with those of studies in Poland and China, which showed that IgAN was the most common diagnosis in patients with nephritic syndrome[4,5,12].

The comparison between patients with and without diabetes showed that both groups frequently presented with asymptomatic proteinuria and nephrotic syndrome. Patients with diabetes most commonly had DN, whereas those without diabetes were primarily diagnosed with LN. These findings are consistent with those of previous studies in Oman, which showed that most patients with diabetes were diagnosed with DN[13]. The comparison between patients with low and normal C3 levels showed that most patients with LN had low C3 levels, consistent with the known

Table 5. Renal biopsy pathology classified by patients with low and normal complement 3 levels

Biopsy (n, %)	Total (n=260)	Normal C3 (n=178)	Low C3 (n=82)	p-value
ANCA-related GN	2 (0.8)	-	2 (1.1)	1.000 [b]
ATN	3 (1.2)	2 (1.1)	1 (1.2)	1.000 [b]
Diffuse glomerulosclerosis	4 (1.5)	2 (1.1)	2 (2.4)	0.593 [b]
DN	57 (21.9)	53 (29.8)	4 (4.9)	<0.001 [a]
FSGS	22 (8.5)	18 (10.1)	4 (4.9)	0.159 [a]
HIVICK	2 (0.8)	2 (1.1)	-	1.000 [b]
IgA nephropathy	58 (22.3)	54 (30.3)	4 (4.9)	<0.001 [a]
LN	78 (30.0)	22 (12.4)	56 (68.3)	<0.001 [a]
MCD	12 (4.6)	11 (6.2)	1 (1.2)	0.111 [b]
MN	12 (4.6)	11 (6.2)	1 (1.2)	0.111 [b]
MPGN	4 (1.5)	3 (1.7)	1 (1.2)	1.000 [b]
PIGN	4 (1.5)	2 (1.1)	2 (2.4)	0.593 [b]
Renal amyloidosis	6 (2.3)	5 (2.8)	1 (1.2)	0.668 [b]
TMA	3 (1.2)	-	3 (3.7)	0.031 [b]
Tubulointerstitial disease	3 (1.2)	1 (0.6)	2 (2.4)	0.235 [b]
Other	7 (2.7)	3 (1.7)	4 (4.9)	0.212 [b]

The p-value by [a] Pearson Chi-square test; [b] Fisher exact test, significant level at p<0.05

Table 6. Renal biopsy pathology classified by patients with nephrotic range proteinuria and sub-nephrotic-range proteinuria

Biopsy (n, %)	Total (n=372)	Sub-nephrotic range proteinuria (UPCR <3.5) (n=193)	Nephrotic range proteinuria (UPCR ≥3.5) (n=179)	p-value
ANCA-related GN	2 (0.5)	2 (1.0)	-	0.499 [b]
ATN	4 (1.1)	2 (1.0)	2 (1.1)	1.000 [b]
Diffuse glomerulosclerosis	9 (2.4)	5 (2.6)	4 (2.2)	1.000 [b]
DN	83 (22.3)	20 (10.4)	63 (35.2)	<0.001 [a]
FSGS	46 (12.4)	28 (14.5)	18 (10.1)	0.192 [a]
HIVICK	2 (0.5)	1 (0.5)	1 (0.6)	1.000 [b]
IgA nephropathy	82 (22.0)	67 (34.7)	15 (8.4)	<0.001 [a]
LN	90 (24.2)	48 (24.9)	42 (23.5)	0.752 [a]
MCD	22 (5.9)	9 (4.7)	13 (7.3)	0.288 [a]
MN	16 (4.3)	4 (2.1)	12 (6.7)	0.028 [a]
MPGN	9 (2.4)	5 (2.6)	4 (2.2)	1.000 [b]
PIGN	4 (1.1)	1 (0.5)	3 (1.7)	0.355 [b]
Renal amyloidosis	9 (2.4)	2 (1.0)	7 (3.9)	0.094 [b]
TMA	3 (0.8)	2 (1.0)	1 (0.6)	1.000 [b]
Tubulointerstitial disease	3 (0.8)	1 (0.5)	2 (1.1)	0.519 [b]
Other	10 (2.7)	6 (3.1)	4 (2.2)	0.752 [b]

The p-value by [a] Pearson Chi-square test; [b] Fisher-Freeman-Halton exact test, significant level at p<0.05

association between SLE and low C3 levels. In contrast, DN and IgAN were more commonly observed in patients with normal C3 levels. Furthermore, the comparison between patients with nephrotic and sub-nephrotic-range proteinuria showed that DN and MN were more frequently observed in patients with nephrotic-range proteinuria. This finding is consistent with that of a Turkish study, which showed that patients with DN had nephrotic-range proteinuria[14]. Conversely, IgAN was more commonly observed in patients with sub-nephrotic-range proteinuria.

The present study identified a total of four cases of acute tubular necrosis (ATN), including two cases in patients presenting with asymptomatic proteinuria, one case in a patient with RPGN, and one case in a patient with CGN. Although ATN is not primarily a glomerular pathology, its occurrence in these clinical settings suggests a complex interplay between glomerular injury and tubular dysfunction[15]. In the case of RPGN, severe glomerular

capillary injury can lead to ischemia and subsequent tubular necrosis due to compromised renal perfusion. Additionally, inflammatory mediators and immune complex deposition associated with RPGN may directly contribute to tubular injury. In patients with CGN, prolonged proteinuria can result in tubular overload, oxidative stress, and apoptosis, predisposing to ATN. Furthermore, CGN is often associated with an increased risk of superimposed acute kidney injury (AKI) due to factors such as volume depletion, nephrotoxic medications, or infections. The occurrence of ATN in patients with asymptomatic proteinuria suggests that even mild glomerular injury may induce tubular stress and dysfunction, possibly through subclinical hemodynamic changes or tubular protein overload. These findings indicate a potential link between severe glomerular injury, tubular stress, and the development of ATN in proteinuria-presenting patients.

Additionally, pathological biopsy findings revealed DN in one patient presenting with RPGN and another patient presenting with nephritic syndrome. These clinical manifestations are atypical for DN, suggesting possible secondary contributing factors[16]. One potential explanation is the coexistence of other glomerular diseases superimposed on underlying DN, such as IgA nephropathy or lupus nephritis, which may present with RPGN or nephritic syndrome. Alternatively, DN can lead to glomerular hyperfiltration and hypertension, increasing the risk of glomerular capillary injury and crescent formation, thereby mimicking the clinical presentation of RPGN. Acute intercurrent events, including infections, hypertensive crises, or exposure to nephrotoxic agents, may also trigger acute inflammation and hematuria, leading to nephritic syndrome-like presentations in DN patients. Additionally, severe proteinuria and glomerular basement membrane thickening in advanced DN may induce inflammatory responses, contributing to atypical clinical manifestations.

These findings underscore the complexity of clinical presentations in DN and highlight the need for kidney biopsy in atypical cases to establish accurate diagnoses. Moreover, the present study suggests a significant interplay between glomerular injury and tubular dysfunction in the development of ATN, emphasizing the need for a comprehensive approach in managing glomerular diseases complicated by ATN. Further research is warranted to elucidate the underlying mechanisms and to optimize diagnostic and therapeutic strategies for these complex clinical scenarios.

The present study has several limitations that should be considered when interpreting the results. First, as a retrospective study, it is subject to inherent biases such as incomplete or inaccurate medical records, which could affect the reliability and accuracy of the data. Reliance on medical records for data collection may also introduce errors or omissions, potentially leading to misclassification or incomplete data sets. Second, this was a single-center study and biopsy indications may vary among different hospitals. Additionally, socioeconomic, genetic, and environmental factors could differ across regions, potentially limiting the generalizability of the findings to other healthcare settings or populations. Furthermore, this study was conducted in an urban setting in Thailand, and the predominance of female participants may limit the applicability of the findings to male patients or other demographic groups. Caution should be exercised when generalizing the results to other regions due to potential differences in occupation, genetics, socioeconomic status, diet, and environmental factors. Third, the study included only patients who underwent renal biopsy, excluding those without symptoms or who were not screened, which may introduce selection bias and limit the generalizability of the results. Additionally, the exclusion of patients with prior kidney transplantation narrows the applicability of the findings, as these patients may exhibit unique renal pathologies. Fourth, the study did not employ multivariate analyses to control for potential confounders, which could result in spurious associations between clinical manifestations and histopathological findings. Moreover, the study did not provide detailed descriptions of the biopsy techniques or histopathological procedures, potentially affecting the consistency and accuracy of diagnoses. Fifth, the laboratory data presented were limited, excluding relevant biomarkers such as anti-phospholipase A2 receptor antibodies for membranous nephropathy, which could provide a more comprehensive understanding of disease processes. Additionally, although common comorbidities such as diabetes and hypertension were reported, their potential influence on biopsy results and renal disease progression was not explored in detail. Finally, the study lacks follow-up data on long-term renal outcomes, which would be valuable for understanding the prognosis of patients based on biopsy findings. Further studies, including prospective multicenter investigations and long-term follow-up, are warranted to validate and expand on these findings.

Despite these limitations, the strengths of the present study lie in its large sample size, which allowed for sufficient statistical power to analyze the relationship between the clinical manifestations of glomerular disease and histopathological findings in urban community patients. Additionally, the present study included a diverse range of clinical manifestations, particularly among patients with asymptomatic urine abnormalities (hematuria and proteinuria). Furthermore, the study exclusively included patients without prior kidney transplantation, allowing for a more focused analysis of diseases affecting the native

kidney.

Conclusion

Glomerular diseases involve pathological changes in the glomeruli and are frequently encountered in clinical practice. Glomerular diseases can lead to chronic kidney disease and end-stage renal disease if left undiagnosed or improperly treated, requiring renal replacement therapy. Diagnosing glomerular disease requires a renal biopsy to assess the pathology, guide treatment, and predict prognosis. Clinical manifestations of glomerulonephritis differ and exhibit varied biopsy pathologies, which also differ across regions and countries. The findings of the present study provide valuable insights into improving diagnostic accuracy in urban community settings.

What is already known on this topic?

Clinical manifestations of glomerular diseases are often associated with specific renal biopsy findings. The prevalence and patterns of clinical manifestations and underlying glomerular diseases vary across populations and geographic regions.

What this study adds?

Asymptomatic proteinuria is the primary indication for renal biopsy in urban Thailand, followed by nephrotic and nephritic syndrome. Lupus nephritis and IgA nephropathy are the most frequent histopathological diagnoses. IgA nephropathy is commonly observed in patients with asymptomatic hematuria, nephritic syndrome, and chronic glomerulonephritis, whereas diabetic nephropathy is associated with asymptomatic proteinuria. LN is prevalent among patients with nephrotic syndrome and rapidly progressive glomerulonephritis. These findings provide valuable insights into improving diagnostic accuracy in urban settings.

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Conflicts of interest

The authors declare no conflict of interest.

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