

Clinicopathological Features of Nondiabetic Renal Diseases from Different Age Groups: An Observational Cross-sectional Study

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Abstract

Background: Diabetes mellitus (DM) has become the leading cause of chronic kidney disease (CKD). Nondiabetic renal diseases (NDRDs) have different clinicopathological features and prognosis from those of diabetic nephropathy. Our study sought to analyze the clinical and pathological features of NDRDs, in different age groups through a cross-sectional study.

Methods: All patients with type 2 DM at our center who underwent renal biopsy between March 1997 and March 2017 were screened and divided into three groups by age: Group 1 (youth group), 18–44 years old; Group 2 (middle-aged group), 45–59 years old; and Group 3 (elderly group), ≥ 60 years old. We analyzed the clinicopathological data and risk factors by univariate and multivariate logistic regression for NDRD of the patients to identify the features of NDRD in different age groups.

Results: We included 982 patients in the final analysis. Patients with NDRD accounted for 64.4% of all patients. IgA nephropathy (IgAN) was the most common pathological pattern in young patients with NDRD, accounting for 26.3%. In the middle-aged group, the two most common pathological patterns were IgAN and membranous nephropathy. Membranous nephropathy was the most common pathological pattern in elderly patients with NDRD, accounting for 29.3%. Consistent with pathological features, glomerular hematuria is a risk factor for NDRD in Group 1 (odds ratio [OR], 26.514; 95% confidence interval [CI], 2.503–280.910; $P = 0.006$). On the other hand, rapidly increasing proteinuria or nephrotic syndrome is a risk factor for NDRD in Group 2 (OR, 5.921; 95% CI, 2.061–17.013; $P = 0.001$) and Group 3 (OR, 90.409; 95% CI, 6.198–1318.826; $P = 0.001$).

Conclusions: This single-center study showed that the proportion and composition of NDRD differ among different age groups. Consistent with pathological features, some clinical indices such as hematuria and proteinuria showed different features among different age groups.

Key words: Age; Nondiabetic Renal Disease; Type 2 Diabetic Nephropathy

INTRODUCTION

With the developments in society and changes in lifestyle, diabetes mellitus (DM) has become one of the most important metabolic diseases. Data from the International Diabetes Federation Diabetes Atlas (8th edition) show that the number of patients with DM in China has reached 144.4 million, the highest worldwide.^[1] Meanwhile, the morbidity of diabetic kidney disease in the DM population was around 35–40% according to the National Health and Nutrition Examination Surveys from 1988 to 2014 in the United States.^[2] Thus, type 2 DM has become the most common cause of chronic kidney disease (CKD).^[3]

The renal biopsy results for CKD in patients with DM could be divided into two categories: Diabetic nephropathy (DN)

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and nondiabetic renal disease (NDRD). There are differences in pathology and prognosis between DN and NDRD, and it is generally believed that NDRD can be improved whereas DN is often difficult to reverse.^[4] Renal biopsy is the gold standard for the diagnosis of DN and NDRD. Thus, our diagnostic standards for NDRD and DN are based on renal biopsy to ensure preciseness.

Many studies have investigated the features and differences of DN and NDRD, most of which sought to identify the influence of some risk factors for DN or NDRD, such as diabetic retinopathy (DR), course of DM, and hematuria.^[5-7] On the other hand, with the developments in society and health care, the number of elderly patients and the incidence of renal biopsies are increasing annually,^[8] prolonging the course of some chronic diseases, and changing the spectrum of the pathological patterns of CKD. Therefore, we wanted to identify the pathological and clinical features of NDRD, in different age groups to offer more information for the management of patients with CKD and DM.

METHODS

Ethical approval

The renal biopsy standards for DM at our hospital follow the Kidney Disease Outcomes Quality Initiative clinical practice guidelines published in 2007.^[9] This study was conducted in accordance with the *Declaration of Helsinki* and approved by the Medicine Ethics Committee of the Chinese People's Liberation Army General Hospital (No. S2014-012-01). All patients provided written informed consent.

Patient selection and experimental design

We retrospectively screened all patients with type 2 DM who underwent renal biopsy at our hospital from March 1997 to 2017. The inclusion criteria were (i) age at renal biopsy >18 years, (ii) clear pathological results of renal biopsy, and (iii) type 2 DM. The exclusion criteria were (i) incomplete medical history or clinical examination results; (ii) serious infection, tumor, and other serious conditions; and (iii) pathological results indicating DN combined with NDRD. All patients were divided into three groups according to pathological pattern: DN or NDRD. To investigate the characteristics of patients with NDRD across different age groups, the patients were divided into three groups according to age: Group 1 (youth group), 18–44 years old ($n = 198$); Group 2 (middle-aged group), 45–59 years old ($n = 299$); and Group 3 (elderly group), ≥ 60 years old ($n = 135$). There are some differences and similarities in disease progression, treatment, and prognosis between DN and NDRD. For a better understanding of the features of NDRD, we analyzed the characteristics of patients with NDRD separately and in comparison with those of patients with DN.

Standard of diagnosis

The diagnosis of type 2 DM was consistent with the 1998 World Health Organization standard.^[10]

DN was diagnosed based on histopathological features such as glomerular hypertrophy, capillary basement membrane thickening, diffuse mesangial expansion, nodular mesangial sclerosis, and hyalinization of afferent and efferent arterioles.^[11] The pathological findings of all patients were reviewed by two experienced nephrologists.

DR was detected using ophthalmology fundus photography or fundus fluorescein angiography. The diagnostic criteria used were in line with the 2017 American Diabetes Association Guidelines.^[12]

Data collection

The following information was collected at the time of renal biopsy: name, sex, age, identification number, medical history of DM, body mass index (BMI), and blood pressure including systolic blood pressure and diastolic blood pressure; complications such as DR, hematuria,^[13] and hypertension; and laboratory indicators, such as hemoglobin level, serum creatinine level, estimated glomerular filtration rate (eGFR, using chronic kidney disease epidemiology collaboration [CKD-EPI] formula for calculation),^[14] and osmotic pressure of urine (UOSM). All collected data are listed and compared between groups in Tables 1 and 2.

Statistical methods

Statistical analysis was performed using SPSS (version 20.0; SPSS Inc., Chicago, IL, USA). Variables with continuous and normal distributions were expressed as a mean \pm standard deviation (SD), and differences between groups were compared using analysis of variance or *t*-test. Multiple comparisons adopted the least significant difference method. Variables with continuous and skewed distributions were represented by median (Q_1 , Q_3), and differences between the analysis groups were compared using the Kruskal–Wallis test or Mann–Whitney *U*-test. Qualitative data were expressed as absolute values and percentages and compared using the Chi-square test. Univariate and multivariate logistic regression analyses were performed to identify the differential prognostic ability of the clinical indices for the development of NDRDs in patients with diabetes, with results reported as odds ratios (ORs) and 95% confidence intervals (CIs). Two-sided $P < 0.05$ was considered to indicate a statistically significant difference.

RESULTS

Sample description

A total of 982 individuals were finally enrolled, comprising 350 patients with DN and 632 patients with NDRD. The age of the patients ranged from 19 to 85 years. The main clinical data of the three groups of NDRD are listed in Table 1. We observed that systolic blood pressure, proteinuria, diabetes course, and the combination of nephrotic syndrome (NS) and cardiovascular and cerebrovascular diseases, all showed an increasing trend with increasing age ($P < 0.05$) in patients with NDRD. In contrast, BMI, serum uric acid, UOSM, hemoglobin level, eGFR, and serum albumin level all showed a decreasing trend with increasing age ($P < 0.05$).

Table 1: Baseline characteristics of patients with NDRD in different age groups

Variables	Total (n = 632)	Group 1 (n = 198)	Group 2 (n = 299)	Group 3 (n = 135)	Statistics	P
Age (years)	49.9 ± 11.6	36.3 ± 5.7	51.7 ± 4.2	65.6 ± 4.7	9.942*	<0.001
Sex (male), n (%)	411 (65.0)	145 (73.2)	195 (65.2)	71 (52.6)	15.046†	0.001
SBP (mmHg)	160.5 ± 26.8	153.50 ± 28.1	161.1 ± 26.2	169.3 ± 23.4	2.924*	<0.001
DBP (mmHg)	98.4 ± 18.4	98.4 ± 21.1	98.5 ± 16.9	98.1 ± 17.4	5.386*	0.975
DM course (months)	25.50 (4.00, 72.00)	16.50 (2.00, 48.0)	32.00 (5.00, 84.00)	48.00 (8.00, 120.00)	27.809‡	<0.001
HbA1c (%)	6.85 ± 1.30	6.92 ± 1.43	6.89 ± 1.31	6.67 ± 1.05	3.346*	0.215
FBG (mmol/L)	6.19 ± 2.03	6.39 ± 2.15	6.17 ± 2.01	5.92 ± 1.87	0.958*	0.117
BMI (kg/m ²)	27.3 ± 3.9	28.2 ± 4.2	27.0 ± 3.6	26.3 ± 3.7	3.372*	<0.001
Hemoglobin (g/L)	134.0 ± 22.1	140.5 ± 22.8	133.8 ± 21.4	125.0 ± 19.3	0.565*	<0.001
Scr (mg/dl)	88.10 (66.20, 122.40)	83.50 (65.38, 115.50)	87.90 (66.90, 124.00)	92.15 (66.35, 134.38)	1.796‡	0.407
ALB (g/L)	33.6 ± 9.3	37.5 ± 8.9	32.6 ± 9.1	30.1 ± 8.5	2.574*	<0.001
UOSM (mOsm/L)	599.47 ± 199.32	675.78 ± 223.48	582.79 ± 180.71	521.89 ± 161.99	10.174*	<0.001
BUA (mol/L)	357.75 ± 105.68	376.28 ± 107.25	354.60 ± 104.57	337.52 ± 102.05	0.110*	0.003
Proteinuria (g/24 h)	2.4 (0.9, 4.9)	1.8 (0.7, 4.2)	2.6 (1.0, 5.7)	3.2 (1.3, 6.1)	15.824‡	<0.001
eGFR (ml·min ⁻¹ ·1.73 m ⁻²)	86.6 ± 26.0	98.6 ± 23.3	84.9 ± 25.0	72.7 ± 24.1	0.371*	<0.001
Family history of DM, n (%)	165 (26.1)	59 (29.8)	89 (29.8)	17 (12.6)	16.254†	<0.001
NS, n (%)	236 (37.3)	46 (23.2)	121 (40.5)	69 (51.1)	29.035†	<0.001
Glomerular hematuria, n (%)	174 (29.0)	50 (26.3)	86 (30.3)	38 (30.4)	1.009†	0.604
DR, n (%)	54 (11.7)	11 (7.7)	29 (13.2)	14 (14.1)	3.184†	0.204
CCVDs, n (%)	102 (16.1)	10 (5.1)	53 (17.7)	39 (28.9)	34.758†	<0.001

Values were shown as median (Q₁, Q₃), mean ± SD, or n (%). *Variance analysis; †Chi-square test; ‡Kruskal–Wallis test. Group 1: Youth group (18–44 years old); Group 2: Middle-aged group (45–59 years old); Group 3: Elderly group (≥60 years old). BMI: Body mass index; DM: Diabetes mellitus; DR: Diabetic retinopathy; CCVDs: Cardiovascular and cerebrovascular diseases; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; ALB: Albumin; HbA1c: Hemoglobin A1c; eGFR: Estimated glomerular filtration rate; UOSM: Osmotic pressure of urine; BUA: Blood uric acid; NS: Nephrotic syndrome; Scr: Serum creatinine; SD: Standard deviation; NDRD: Nondiabetic renal disease; FBG: Fasting blood glucose.

Compared with DN, NDRD showed different features among different age groups [Table 2]. We found that the BMI of patients with NDRD was higher than that of patients with DN among the three groups; however, the difference was statistically significant only in Groups 1 and 2 ($P < 0.05$). Proteinuria level was lower in patients with NDRD than in those with DN among the three groups; however, the difference was statistically significant only in Groups 1 and 2. The incidence of NS showed the same trend as that of proteinuria level. The albumin level of patients with NDRD was lower than that of patients with DN in Group 1 but higher than that of patients with DN in Group 3 ($P < 0.05$). The systolic blood pressure and diabetes course of patients with DN were higher and longer, respectively, than those of patients with NDRD among the three groups ($P < 0.05$). On the other hand, hemoglobin, UOSM, eGFR, and the incidence of glomerular hematuria were lower in patients with DN than in those with NDRD among the three groups ($P < 0.05$).

Pathological patterns among different age groups

Patients with NDRD accounted for 64.4% of all patients with DM who underwent renal biopsy. The incidence of NDRD was the highest in Group 1 (70.5%), second in Group 3 (64.9%), and the lowest in Group 2 (60.6%); however, the difference was statistically significant only between Groups 2 and 1 ($P = 0.006$).

We analyzed the composition of pathological patterns in patients with NDRD, and the results are shown in Table 3. IgA nephropathy (IgAN) and membranous nephropathy

were the two most common patterns among patients with NDRD. The proportion of IgAN decreased with age whereas the proportion of membranous nephropathy increased with age ($P < 0.05$).

In Group 1, the most common pathological pattern of NDRD was IgAN, accounting for 37.4%. Subsequently, membranous nephropathy accounted for 16.2%. In Group 2, the most common pathological pattern of NDRD was membranous nephropathy, accounting for 33.8%; the second was IgAN, accounting for 32.1%. In Group 3, the most common pathological pattern of NDRD was membranous nephropathy, accounting for 45.2%; the second was IgAN, which accounted for 20.7%.

Risk factors for nondiabetic renal disease among different age groups

A single-factor logistic regression was performed to screen for potential independent risk factors for NDRD in each of the three groups, and the results are listed in Table 4. Then, we included all potential independent risk factors for NDRD in a multivariate logistic regression (forward stepwise method) of the three groups. The absence of DR showed a good correlation with NDRD in all three groups. Hemoglobin and shorter DM course had high ORs (1.051 and 1.033, 0.977 and 0.986, respectively) for NDRD in Groups 1 and 2. Rapidly increasing proteinuria level or NS showed a good correlation with NDRD in both groups 2 and 3 (OR , 5.921 or 90.409). Hematuria had a high OR (26.514) for NDRD in Group 1. Systemic disease and family history of DM showed a good correlation with NDRD in Group 3.

Table 2: Comparison of nondiabetic renal disease and diabetic nephropathy in different age groups

Variables	Group 1 (n = 281)			
	DN (n = 83)	NDRD (n = 198)	Statistics	P
SBP (mmHg)	174.6 ± 25.3	153.5 ± 28.1	5.902*	<0.001
DM course (months)	96.00 (36.00, 132.00)	16.50 (2.00, 48.00)	3048.500‡	<0.001
HbA1c (%)	7.08 ± 1.79	6.92 ± 1.43	0.747*	0.456
BMI (kg/m ²)	26.79 ± 3.96	28.23 ± 4.23	-2.559*	0.011
Hemoglobin (g/L)	112.24 ± 22.91	140.46 ± 22.82	-9.362*	<0.001
ALB (g/L)	32.13 ± 6.13	37.51 ± 8.90	-5.820*	<0.001
BUA (μmol/L)	376.99 ± 84.91	376.28 ± 107.25	0.054*	0.957
UOSM (mOsm/L)	492.67 ± 191.89	675.78 ± 223.48	-6.044*	<0.001
Proteinuria (g/24 h)	4.29 (2.15, 7.42)	1.79 (0.67, 4.19)	4632.500‡	<0.001
eGFR (ml·min ⁻¹ ·1.73 m ⁻²)	77.89 ± 26.76	98.59 ± 23.29	-6.495*	<0.001
Family history of DM, n (%)	47 (56.6)	59 (74.7)	17.918†	<0.001
NS, n (%)	30 (36.1)	46 (23.2)	4.942†	0.026
Glomerular hematuria, n (%)	5 (6.6)	50 (26.3)	12.893†	<0.001
DR, n (%)	60 (77.9)	11 (32.4)	112.221†	<0.001
CCVDs, n (%)	12 (14.5)	10 (5.1)	7.172†	0.007
Variables	Group 2 (n = 493)			
	DN (n = 194)	NDRD (n = 299)	Statistics	P
SBP (mmHg)	182.2 ± 23.5	161.1 ± 26.2	9.116*	<0.001
DM course (months)	156.00 (78.75, 192.00)	32.00 (5.00, 84.00)	9105.500‡	<0.001
HbA1c (%)	7.05 ± 1.43	6.89 ± 1.31	1.247*	0.213
BMI (kg/m ²)	26.26 ± 3.68	27.04 ± 3.60	-2.303*	0.022
Hemoglobin (g/L)	112.97 ± 20.59	133.78 ± 21.04	-10.606*	<0.001
ALB (g/L)	32.20 ± 6.22	32.57 ± 9.10	-0.526*	0.599
BUA (μmol/L)	367.53 ± 81.40	354.60 ± 104.57	1.535*	0.125
UOSM (mOsm/L)	474.16 ± 150.90	582.79 ± 180.71	-6.527*	<0.001
Proteinuria (g/24 h)	3.64 (2.07, 5.73)	2.64 (1.02, 5.74)	24087.000‡	0.001
eGFR (ml·min ⁻¹ ·1.73 m ⁻²)	71.90 ± 22.68	84.85 ± 24.95	-5.835*	<0.001
Family history of DM, n (%)	79 (40.7)	89 (29.8)	6.287†	0.012
NS, n (%)	64 (33.0)	121 (40.5)	2.807†	0.094
Glomerular hematuria, n (%)	10 (5.6)	86 (30.3)	40.434†	<0.001
DR, n (%)	141 (78.3)	29 (13.2)	171.960†	<0.001
CCVDs, n (%)	62 (32.0)	53 (17.7)	13.327†	<0.001
Variables	Group 3 (n = 208)			
	DN (n = 73)	NDRD (n = 135)	Statistics	P
SBP (mmHg)	187.3 ± 19.3	169.3 ± 23.4	5.644*	<0.001
DM course (months)	156.00 (84.00, 222.00)	48.00 (8.00, 120.00)	2177.500‡	<0.001
HbA1c (%)	6.91 ± 1.29	6.67 ± 1.05	1.409*	0.160
BMI (kg/m ²)	25.72 ± 2.97	26.25 ± 3.66	-1.057*	0.292
Hemoglobin (g/L)	111.04 ± 21.14	125.00 ± 19.32	-4.790*	<0.001
ALB (g/L)	33.41 ± 5.33	30.12 ± 8.45	3.393*	0.001
BUA (μmol/L)	364.98 ± 90.08	337.52 ± 102.05	1.928*	0.055
UOSM (mOsm/L)	446.63 ± 112.38	521.89 ± 161.99	-3.396*	0.001
Proteinuria (g/24 h)	3.77 (1.80, 5.99)	3.19 (1.29, 6.13)	4465.000‡	0.301
eGFR (ml·min ⁻¹ ·1.73 m ⁻²)	65.84 ± 19.93	72.66 ± 24.14	-2.063*	0.04
Family history of DM, n (%)	25 (34.2)	17 (12.6)	13.786†	<0.001
NS, n (%)	22 (30.1)	69 (51.1)	8.470†	0.004
Glomerular hematuria, n (%)	5 (7.4)	38 (30.4)	13.510†	<0.001
DR, n (%)	53 (77.9)	14 (14.1)	68.301†	<0.001
CCVDs, n (%)	29 (39.7)	39 (28.9)	2.529†	0.112

Values were shown as median (Q₁, Q₃), mean ± SD, or n (%). *Student's *t*-test; †Chi-square test; ‡Mann-Whitney test. Group 1: Youth group (18–44 years old); Group 2: Middle-aged group (45–59 years old); Group 3: Elderly group (≥60 years old). BMI: Body mass index; DM: Diabetes mellitus; DR: Diabetic retinopathy; CCVDs: Cardiovascular and cerebrovascular diseases; SBP: Systolic blood pressure; ALB: Albumin; HbA1c: Hemoglobin A1c; eGFR: Estimated glomerular filtration rate; UOSM: Osmotic pressure of urine; BUA: Blood uric acid; NS: Nephrotic syndrome; Scr: Serum creatinine; SD: Standard deviation; DN: Diabetic nephropathy; NDRD: Nondiabetic renal disease.

Table 3: Distribution of pathological patterns of NDRD

Pathological diagnosis	Total (n = 632)	Group 1 (n = 198)	Group 2 (n = 299)	Group 3 (n = 135)	χ^2	P
IgAN	198 (31.3)	74 (37.4)	96 (32.1)	28 (20.7)	10.482	0.005
MN	194 (30.7)	32 (16.2)	101 (33.8)	61 (45.2)	34.320	<0.001
Obesity-related glomerulopathy	31 (4.9)	22 (11.1)	9 (3.0)	0 (0)	25.614	<0.001
FSGS	52 (8.2)	19 (9.6)	27 (9.0)	6 (4.4)	3.305	0.192
Minimal change glomerulopathy	30 (4.7)	9 (4.5)	11 (3.7)	10 (7.4)	2.885	0.236
Mesangial proliferative glomerulonephritis	42 (6.6)	11 (5.6)	16 (5.4)	15 (11.1)	5.526	0.063
Hypertensive renal damage	35 (5.5)	14 (7.1)	16 (5.4)	5 (3.7)	1.777	0.411
Amyloid nephropathy	19 (3.0)	2 (1.0)	14 (4.7)	3 (2.2)	5.871	0.053
Hepatitis B virus associated Glomerulonephritis	21 (3.3)	6 (3.0)	9 (3.0)	6 (4.4)	0.672	0.714
ANCA-associated vasculitis and glomerulonephritis	3 (0.4)	1 (0.5)	0 (0)	2 (1.5)	4.326	0.115

Values were shown as n (%). NDRD: Nondiabetic renal disease; ANCA: Anti neutrophil cytoplasmic antibody; MN: Membranous nephropathy; IgAN: IgA nephropathy; FSGS: Focal segmental glomerular sclerosis.

Table 4: Risk factors for NDRD among different age groups

Variables	Group 1 (n = 198)			Group 2 (n = 299)			Group 3 (n = 135)		
	OR	95% CI	P	OR	95% CI	P	OR	95% CI	P
Univariate logistic regression analysis									
DR	0.024	0.011–0.054	<0.001	0.042	0.025–0.071	<0.001	0.047	0.021–0.104	<0.001
SBP	0.973	0.963–0.983	<0.001	0.968	0.960–0.976	<0.001	0.962	0.947–0.977	<0.001
DM course	0.973	0.967–0.980	<0.001	0.980	0.977–0.984	<0.001	0.988	0.984–0.992	<0.001
Rapidly increasing proteinuria or nephrotic syndrome	2.335	1.186–4.594	0.014	12.318	6.381–23.778	<0.001	7.362	3.231–16.772	<0.001
Hemoglobin	1.051	1.037–1.065	<0.001	1.045	1.035–1.056	<0.001	1.035	1.019–1.051	<0.001
Glomerular hematuria	5.071	1.937–13.28	0.001	7.297	3.673–14.495	<0.001	5.503	2.051–14.769	0.001
Family history of DM	0.325	0.191–0.553	<0.001	0.617	0.422–0.901	0.012	0.227	0.137–0.558	<0.001
Hypertension	0.265	0.115–0.623	0.002	0.159	0.067–0.379	<0.001	–	–	–
Systemic disease	–	–	–	2.058	1.164–3.639	0.013	4.514	1.517–13.432	0.007
ALB	1.077	1.044–1.112	<0.001	–	–	–	0.943	0.905–0.981	0.004
Multivariate logistic regression analysis									
DR	0.031	0.007–0.137	<0.001	0.102	0.045–0.230	<0.001	0.007	0.001–0.079	0.007
Systemic disease	–	–	–	–	–	–	30.237	1.836–498.094	0.017
DM course	0.977	0.963–0.992	0.002	0.986	0.980–0.991	<0.001	–	–	–
Rapidly increasing proteinuria or NS	–	–	–	5.921	2.061–17.013	0.001	90.409	6.198–1318.826	0.001
Family history of DM	–	–	–	–	–	–	0.027	0.002–0.389	0.008
Hemoglobin	1.051	1.021–1.082	0.001	1.033	1.014–1.051	<0.001	–	–	–
Glomerular hematuria	26.514	2.503–280.91	0.006	–	–	–	–	–	–

Group 1: Youth group (18–44 years old); Group 2: Middle-aged group (45–59 years old); Group 3: Elderly group (≥ 60 years old). OR: Odds ratio; CI: Confidence interval; DR: Diabetic retinopathy; SBP: Systolic blood pressure; DM: Diabetes mellitus; ALB: Albumin; NS: Nephrotic syndrome; –: Not available; NDRD: Nondiabetic renal disease.

DISCUSSION

Currently, DM has surpassed glomerulonephritis as the leading cause of predialysis CKD.^[15] Furthermore, the human life expectancy has increased with societal developments, increasing the proportion of elderly people. In China, the population of persons >60 years old has already reached 177 million.^[8] Thus, it is necessary to analyze the clinical and pathological features of NDRD across different age groups considering that aging is related to CKD and DM.

Our study found that the prevalence of NDRD in patients with type 2 diabetic kidney disease in China is 64.4%. On the other hand, according to our literature research, the

prevalence ranges from 17.4% to 61.29% among different studies [Supplementary Table 1]. The discrepancy might be related to differences in ethnicity, inclusion criteria, proportion of patients undergoing kidney biopsy, sample size, and other factors. Our study found that the incidence of NDRD was also different across different age groups ($P < 0.05$), with the youth group showing the highest incidence, followed by the elderly group and then the middle-aged group. Thus, the different age composition of different studies might also be one reason for the different NDRD prevalence in the literature.

The proportion of pathological patterns was also different among different studies on NDRD [Supplementary Table 1].

Some showed that the most common pathological pattern in patients with NDRD was IgAN whereas membranous nephropathy, hypertensive renal disease, focal segmental glomerular sclerosis, and acute interstitial nephritis were also reported as the most common pathological pattern in other studies [Supplementary Table 1]. This difference might also be related to the inconsistency in the age composition. IgAN is one of the most common types of primary glomerulonephritis, the incidence rate of which varies from 32% to 54% in patients with primary glomerulonephritis in China.^[16] Our study showed that IgAN accounted for 26.3% of patients in Group 1 but only 19.5% in Group 3. This might be because IgAN mostly develops in young and middle-aged patients.^[17,18] In our study, membranous nephropathy was the most common pathological pattern of NDRD in Group 3 (29.3%), which was also consistent with the higher prevalence of NS in elderly patients. Some studies showed that membranous nephropathy is the most common pathological pattern in patients >60 years old with CKD, accounting for 39.6%.^[17] Moreover, its incidence increases annually. This might be due to developments in medicine that encourage increasingly more elderly patients to undergo renal biopsy. On the other hand, with the increase in life expectancy, the proportion of elderly patients with CKD also increases.^[17]

Corresponding with the pathological pattern, some clinical indices also showed different correlations with NDRD in different age groups. Hematuria had a higher *OR* in Group 1 than in Groups 2 and 3. This may be because the main pathological pattern of NDRD in Group 1 was IgAN, with hematuria as one of the main clinical features.^[19] Similarly, rapidly increasing proteinuria level or NS had a higher *OR* in Groups 2 and 3 than in Group 1. This might be because a high level of proteinuria is one of the main clinical features of membranous nephropathy,^[20] which was the main pathological pattern in the two groups.

Notably, the absence of DR, which is a widely recognized risk factor for NDRD,^[9,21] had a stable distinguishing ability between DN and NDRD in different age groups in our study. DN and DR share the same pathological mechanisms,^[22] which leads to their consistency.

This study is limited by its single-center and cross-sectional nature. Thus, our results should be further strengthened by a longitudinal follow-up study to provide more clinically relevant information. Despite these limitations, our study still identified that the proportion and composition of NDRD differ among different age groups. In this study, consistent with pathological features, some clinical indices such as hematuria and proteinuria showed different features among different age groups.

Supplementary information is linked to the online version of the paper on the Chinese Medical Journal website.

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Conflicts of interest

There are no conflicts of interest.

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不同年龄组非糖尿病肾脏疾病患者的临床病理特征分析：一项观察性横断面研究

摘要

背景：糖尿病已成为慢性肾脏病的主要原因。和糖尿病肾病相比，非糖尿病肾脏疾病(NDRD, non-diabetic renal disease)有着不同的临床病理特征以及预后。我们的研究旨在分析不同年龄组NDRD患者的临床病理特征。

方法：我们筛选了我中心从1997年至2017年所有的经肾脏病理活检的2型糖尿病患者，并且根据年龄分为3组：组1（青年组），18-44岁；组2（中年组），45-59岁；组3（老年组），大于等于60岁。我们通过单因素及多因素logistic回归分析了NDRD的危险因素来分析不同年龄组NDRD患者的特征。

结果：我们共纳入982人。NDRD患者占比为64.4%。青年组NDRD患者中，IgA肾病是最常见的病理类型，占比为26.3%。在中年组NDRD患者中，膜性肾病和IgA肾病是最常见的两种病理类型。膜性肾病是老年组NDRD患者中最常见的病理类型，占比为29.3%。和病理特征相一致，在青年组中，血尿是NDRD的危险因素。而中年和老年组中，快速增加的蛋白尿或肾病综合征为NDRD的危险因素。

结论：我们单中心研究显示不同年龄组中NDRD的占比及构成比不同。和病理特征相一致，一些临床指标，例如血尿和蛋白尿在不同年龄组中也表现出不同的特征。

Supplementary Table 1: Pathological results of NDRD in different researches

Country/region	Author	Published time	NDRD ratio (%)	The most common pathological type (%)	Sample size
Korea	Lee <i>et al.</i> ^[1]	2017	39.09	MN (41.7)	220
China	Liu <i>et al.</i> ^[2]	2017	36.89	MN (33.06)	188
China	Dong <i>et al.</i> ^[3]	2016	61.29	MN (36.18)	248
Iran	Soleymanian <i>et al.</i> ^[4]	2015	43.50	MN (34)	46
Turkey	Yenigun <i>et al.</i> ^[5]	2015	52.11	FSGS (18.9)	71
China	Yan <i>et al.</i> ^[6]	2015	46.58	HRD (58)	161
Croatia	Horvatic <i>et al.</i> ^[7]	2014	36.25	MN (20.9)	80
Republic of Korea	Oh SW <i>et al.</i> ^[8]	2012	51.59	IgAN (21.05)	126
China	Mou S <i>et al.</i> ^[9]	2009	52.20	FSGS (37.7)	69
Taipei	Lin <i>et al.</i> ^[10]	2009	30	AIN (42.3)	50
Japan	Tone <i>et al.</i> ^[11]	2005	47.42	IgAN (25.8)	97
Hong Kong	Wong <i>et al.</i> ^[12]	2002	46	IgAN (32.26)	68
Spain	Serra <i>et al.</i> ^[13]	2002	17.14	IgAN (50)	35
Hong Kong	Mak <i>et al.</i> ^[14]	1997	33.33	IgAN (59)	51

MN: Membranous nephropathy; IgAN: IgA nephropathy; FSGS: Focal segmental glomerular sclerosis; HRD: Hypertensive renal disease; AIN: Acute interstitial nephritis; NDRD: Nondiabetic renal disease.

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