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Prevalence and Determinants of Diabetic Nephropathy in Korea: Korea National Health and Nutrition Examination Survey

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Background: Diabetic nephropathy is a leading cause of end stage renal disease and is associated with an increased risk of cardiovascular mortality. It manifests as albuminuria or impaired glomerular filtration rate (GFR), and the prevalence of diabetic nephropathy varies with ethnicity. The prevalence of diabetic nephropathy and its determinants in Korean adults have not previously been studied at the national level. This cross-sectional study was undertaken to ascertain the prevalence and determinants of albuminuria and chronic kidney disease (CKD) in Korean patients with diabetes.
Methods: The Korea National Health and Nutrition Examination Survey (KNHANES) V, conducted in 2011, was used to define albuminuria (n=4,652), and the dataset of KNHANES IV–V (2008–2011) was used to define CKD (n=21,521). Selected samples were weighted to represent the entire civilian population in Korea. Albuminuria was defined as a spot urine albumin/creatinine ratio >30 mg/g. CKD was defined as a GFR <60 mL/min/1.73 m^2.
Results: Among subjects with diabetes, 26.7% had albuminuria, and 8.6% had CKD. Diabetes was associated with an approximate 2.5-fold increased risk of albuminuria, with virtually no difference between new-onset and previously diagnosed diabetes. Only systolic blood pressure was significantly associated with albuminuria, and old age, high serum triglyceride levels, and previous cardiovascular disease (CVD) were related with CKD in subjects with diabetes.
Conclusion: Korean subjects with diabetes had a higher prevalence of albuminuria and CKD than those without diabetes. Blood pressure was associated with albuminuria, and age, triglyceride level, and previous CVD were independent determinants of CKD in subjects with diabetes.

Keywords: Albuminuria; Chronic renal disease; Diabetes mellitus; Diabetic nephropathy; Korea

INTRODUCTION

Diabetic nephropathy is the leading cause of end-stage renal disease [1] and is associated with an increased risk of cardiovascular mortality [2-4]. Approximately 40% of persons with diabetes develop diabetic nephropathy, which manifests as al-

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buminuria or reduced glomerular filtration rate (GFR) [5,6]. However, the prevalence of albuminuria varies with ethnicity, with higher rates reported in Asian populations than in Caucasian populations [7,8]. In addition, the prevalence of and risk factors for chronic kidney disease (CKD) demonstrate significant interracial disparities [9,10].

Several studies have reported the incidence and risk factors for diabetic nephropathy in Korean patients with diabetes. In a hospital-based study, Lee et al. [11] and Park et al. [12] reported that 34% of patients with diabetes had albuminuria and that poor glycemic control, high blood pressure, presence of diabetic retinopathy, and duration of diabetes were independently associated with albuminuria. Several studies have also investigated the risk factors for albuminuria, including male sex, hemoglobin A1c (HbA1c), homocysteine, body mass index (BMI), fasting insulin level, and fasting C-peptide level [13-16]. However, the majority of epidemiologic studies are small single center reports or primary clinic based studies, and did not compare subjects with or without diabetes.

Recently, the prevalence of CKD in Korean adults in 2009 was reported to be 4.5% in men and 6.3% in women using data from the Korea National Health and Nutrition Examination Survey (KNHANES) IV [17]. However, the authors did not compare the prevalence of CKD by diabetes status, nor did they investigate the determinants of CKD. Furthermore, to the best of our knowledge, there have been no studies regarding albuminuria using data from KNHANES. Albuminuria was measured for the first time in the most recent version of KNHANES (2011); therefore, we were able to use this dataset to investigate the epidemiology of albuminuria, compared between subjects with or without diabetes.

Therefore, the aim of the present study was to investigate the prevalence and determinants of albuminuria and CKD according to the presence or absence of diabetes using the nationally representative dataset from KNHANES.

METHODS

Study population

KNHANES is a cross-sectional, nationwide survey examining the general health and nutrition status of Korean people. We included subjects aged >30 years and excluded subjects with a missing random urine microalbumin level, fasting plasma glucose level, or previous medical history. Data from KNHANES V, which was conducted in 2011, was used to estimate the prevalence of albuminuria. As a result, the data from 4,652 subjects were used to analyze albuminuria status. The KNHANES IV–V dataset (2008–2011) was used to estimate the prevalence of CKD. Data from 21,521 subjects were used to analyze CKD status.

Definition of diabetes and glucose tolerance categories

Diabetes was defined using the following criteria: 1) new onset diabetes, fasting blood glucose ≥126 mg/dL or HbA1c ≥6.5% that was first detected in our survey; or 2) known diabetes, use of medication to decrease blood glucose levels at the time of the interview or self-report of a previous diagnosis by a physician. Impaired fasting glucose (IFG) was defined as fasting plasma glucose levels in the range 100 to 125 mg/dL.

Definition of albuminuria and CKD

Diabetic nephropathy was defined as diabetes with the presence of albuminuria or impaired GFR. In KNHANES V, which was conducted in 2011, urine albumin and creatinine concentrations were measured using single urine sampling. Urinary albumin was evaluated by turbidimetric assay using a Hitachi Automatic Analyzer 7600 (Hitachi, Tokyo, Japan). Albuminuria was defined as a spot urine albumin/creatinine ratio (ACR) ≥30 mg/g, and the albuminuria categories were as follows: microalbuminuria, ACR 30 to 299 mg/g and macroalbuminuria, ACR ≥300 mg/g. The level of kidney function was determined by estimating the GFR using an abbreviated equation developed from the Modification of Diet in Renal Disease (MDRD) formula: estimated GFR (mL/min/1.73 m^2) = 186.3 × (serum creatinine$^{-1.154}$) × (age$^{-0.203}$) × 0.742 (if female) [18]. We defined CKD as eGFR <60 mL/min/1.73 m^2. The GFR categories were defined using the following criteria: stage 1, GFR ≥90 mL/min/1.73 m^2; stage 2, GFR 60 to 89 mL/min/1.73 m^2; stage 3, 30 to 59 mL/min/1.73 m^2; stage 4, GFR 15 to 29 mL/min/1.73 m^2; and stage 5, GFR <15 mL/min/1.73 m^2.

Other chronic diseases

Hypertension was defined as the presence of either of the following two criteria: 1) systolic blood pressure (SBP) ≥140 mm Hg or diastolic blood pressure ≥90 mm Hg, or 2) use of an antihypertensive medication at the time of the interview. Dyslipidemia was defined as the presence of any of the following three criteria: 1) serum triglyceride ≥200 mg/dL after 12 hours of fasting, 2) serum total cholesterol ≥240 mg/dL, or 3) use of an antidyslipidemic medication at the time of the interview. Cardiovascular disease (CVD) history was self-reported and

included a history of congestive heart failure, coronary heart disease, heart attack, angina, or stroke. Medication history was ascertained using the questionnaire.

Health-related behavior

The amount of pure alcohol consumed (g/day) was calculated using the average number of alcoholic beverages consumed and frequency of alcohol consumption. Respondents who drank >30 g/day were considered heavy drinkers. Regular exercise was defined as strenuous physical activity performed for ≥20 minutes at a time ≥3 times a week. A person was considered a smoker when they were currently smoking and had smoked >100 cigarettes in their lifetime.

Statistical analysis

All data are presented as mean±standard error (SE) for continuous variables or as proportion (SE) for categorical variables. Logarithmic transformation was used for variables with skewed distributions. Statistical analyses were performed using SAS statistical software version 9.3 (SAS Institute Inc., Cary, NC, USA) to reflect the complex sampling design and sampling weights of KNHANES and to provide nationally representative prevalence estimates using a complex sampling design. Differences were analyzed using chi-square tests for categorical variables and Student *t*-tests for the continuous variables. Determinants of albuminuria were analyzed using multivariate logistic regression analysis. The odds ratio (OR) and 95% confidence interval (95% CI) for the factors associated with the presence of albuminuria or CKD were calculated using multivariate logistic regression analysis. A *P* value <0.05 was considered statistically significant.

RESULTS

Clinical characteristics of the study population

Table 1 shows the clinical characteristics of the study population. Of the 4,652 subjects, 660 had diabetes. The mean duration of diabetes was 5.1 years. Age, HbA1c level, fasting plasma glucose concentration, BMI, prevalence of hypertension, and prevalence of dyslipidemia were higher in the subjects with diabetes than in those without diabetes. The ACR was higher, and the GFR was lower, in patients with diabetes than in those without diabetes (geometric mean of ACR, 14.1±0.4 mg/g vs. 5.7±0.7 mg/g, *P*<0.0001; and GFR, 87.4±1.0 mL/min/1.73 m^2 vs. 92.8±0.4 mL/min/1.73 m^2, *P*<0.0001). Alcohol consumption, smoking, and exercise status were not different between the two groups.

Table 1. Clinical characteristics of the study population according to diabetes status

Characteristic	No Diabetes (*n*=3,992)	Diabetes (*n*=660)	*P* value
Age, yr	49.2±0.4	58.8±0.7	<0.001
Male sex[a]	50.1 (0.8)	57.6 (2.1)	0.002
BMI, kg/m^2	23.8±0.1	25.2±0.2	<0.001
WC, cm	81.9±0.2	87.9±0.5	<0.001
SBP, mm Hg	118.3±0.4	127.1±1.0	<0.001
FPG, mg/dL	92.8±0.2	138.0±2.1	<0.001
HbA1c, %	5.5±0.0	7.3±0.1	<0.001
Total cholesterol, mg/dL	193.5±0.7	191.3±2.0	0.299
Triglycerides, mg/dL[b]	113.0 (110.1–116)	146.4 (138–155.3)	<0.001
BUN, mg/dL	14.2±0.1	15.9±0.2	<0.001
Creatinine, mg/dL	0.8±0.0	0.9±0.0	<0.001
GFR, mL/min	92.8±0.4	87.4±1	<0.001
ACR, mg/g[b]	5.7 (5.3–6.0)	14.1 (12.1–16.6)	<0.001
Duration of DM, yr	-	5.1±0.3	-
New onset DM[a]	-	37.3 (2.4)	-
Medication for DM[a]	-	56.8 (2.5)	-
HTN[a]	27.0 (0.9)	56.5 (2.5)	<0.001
Medication for HTN[a]	14.5 (0.7)	45.2 (2.3)	<0.001
Dyslipidemia[a]	22.3 (0.8)	45.6 (2.3)	<0.001
Medication for dyslipidemia[a]	3.6 (0.3)	17.6 (1.8)	<0.001
CVD[a]	2.4 (0.2)	7.6 (1.0)	<0.001
Alcohol consumption[a]	11.7 (0.7)	12.0 (1.6)	0.883
Smoking[a]	24.0 (0.9)	27.7 (2.1)	0.085
Exercise[a]	20.5 (0.8)	16.7 (2.0)	0.065

Values are presented as mean±standard error. BMI was defined as body mass (kg) divided by the square of height (m^2).
BMI, body mass index; WC, waist circumference; SBP, systolic blood pressure; FPG, fasting plasma glucose; HbA1c, hemoglobin A1c; BUN, blood urea nitrogen; GFR, glomerular filtration rate; ACR, albumin creatinine ratio; DM, diabetes mellitus; HTN, hypertension; CVD, cardiovascular disease.
[a]Values are presented as % (standard error), [b]ACR and triglyceride levels are presented as geometric mean (95% confidence interval).

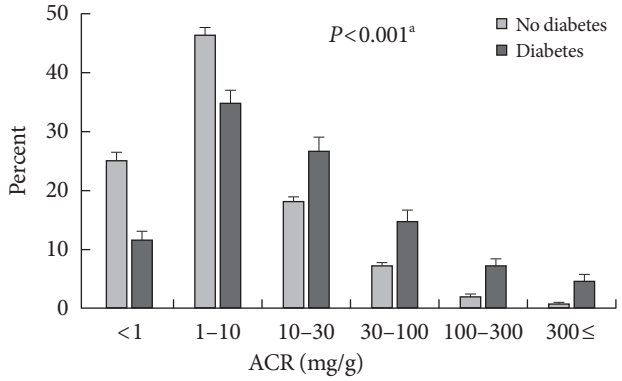

Fig. 1. Distribution of the albumin creatinine ratio (ACR) according to diabetes status. [a]*P* value for the comparison of the proportion of subjects with albuminuria, compared between subjects with and without diabetes.

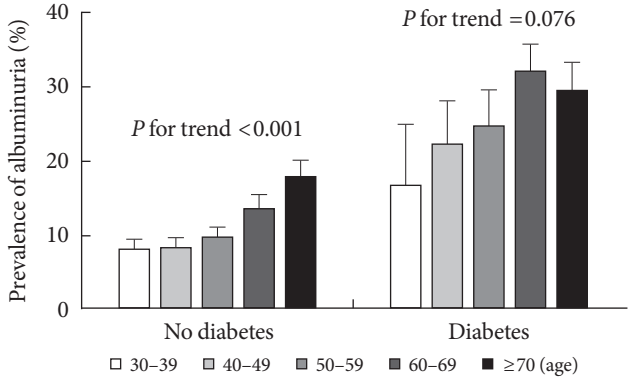

Fig. 2. Prevalence of albuminuria according to age and diabetes status.

Prevalence and determinants of albuminuria according to the diabetes status

Albuminuria was more prevalent in subjects with diabetes than in those without (26.7% vs. 10.2%, $P<0.0001$). The prevalence of microalbuminuria and macroalbuminuria was also higher in subjects with diabetes than in those without (22.0% vs. 9.4% and 4.6% vs. 0.8%, respectively) (Fig. 1). There was a significant trend for increased albuminuria with increasing age in subjects without diabetes (*P* for trend <0.0001), whereas the trend was not statistically significant in subjects with diabetes (*P* for trend=0.076) (Fig. 2). Table 2 shows the clinical characteristics of the study population according to the status of albuminuria and diabetes. In the group without diabetes, subjects with albuminuria were older and had higher BMI, waist circumference (WC), fasting plasma glucose concentration, and SBP than those without diabetes. However, in the group with diabetes, subjects with albuminuria had a higher fasting plasma glucose concentration and SBP. In multiple logistic regression analysis, in the nondiabetic group, BMI and SBP were independent risk factors for albuminuria, whereas, in the diabetic group, only SBP was independently associated with albuminuria (Table 3).

Association between glucose tolerance categories and albuminuria

In the logistic regression analysis to determine the impact of diabetes on albuminuria, subjects with diabetes had an increased risk of albuminuria, compared to those without diabetes (OR, 2.35; 95% CI, 1.78 to 3.10; $P<0.0001$) after adjusting for age, sex, BMI, SBP, exercise, smoking status, and alcohol consumption status. When we categorized the subjects into four groups according to glucose tolerance status and duration of diabetes (normal, IFG, new onset diabetes, and known diabetes), IFG, new onset diabetes, and known diabetes were significant risk factors for albuminuria after adjusting for age and sex (Table 4). However, with further adjustment for BMI and SBP, only new onset diabetes and known diabetes were significantly associated with albuminuria (Table 4).

Prevalence and determinants of CKD according to diabetes status

Table 5 shows the clinical characteristics of the study population according to diabetes status and CKD. Of the 21,521 subjects, 2,436 had diabetes. In subjects without diabetes, 1.7% had CKD with a mean GFR of 51.5±0.6 mL/min/1.73 m^2. In those with diabetes, 8.6% had CKD with a mean GFR of 48.1±1.0 mL/min/1.73 m^2. Subjects with diabetes had a higher stage of CKD than those without diabetes ($P<0.001$) (Fig. 3). In both groups, with and without diabetes, the subjects with CKD were older and had a higher fasting plasma glucose level and higher rates of hypertension, dyslipidemia, and CVD than subjects without CKD. However, the percentage of alcohol consumers, smokers, and exercisers was lower in subjects with CKD than that in subjects without CKD in both groups (Table 5). In the multivariate logistic regression analysis, age, WC, triglyceride concentration, and previous CVD events were associated with an increased risk of CKD in the group without diabetes. In the group with diabetes, age, triglyceride concentration, and diabetes duration were risk factors for CKD. However, total cholesterol concentration, heavy alcohol consumption, and exercise were associated with a lower risk of CKD in the group with diabetes (Table 6).

Table 2. Clinical characteristics of the study population according to the presence/absence of albuminuria and diabetes

Characteristic	No diabetes			Diabetes		
	Normal (*n*=3,599)	Albuminuria (*n*=393)	*P* value	Normal (*n*=480)	Albuminuria (*n*=180)	*P* value
Age, yr	48.9±0.4	52.6±1.0	<0.001	58.1±0.8	60.8±1.2	0.064
Male sex[a]	50.5 (0.8)	47.2 (3.8)	0.406	56.4 (2.5)	61.2 (4.6)	0.391
BMI, kg/m^2	23.8±0.1	24.5±0.2	0.002	25.3±0.2	24.8±0.3	0.212
WC, cm	81.6±0.2	84.3±0.7	<0.001	88.0±0.5	87.6±1	0.714
SBP, mm Hg	117.4±0.4	126.1±1.4	<0.001	124.4±0.9	134.7±1.9	<0.001
FPG, mg/dL	92.6±0.2	94.5±0.7	0.011	135.6±2.5	144.4±3.4	0.032
HbA1c, %	5.5±0.0	5.6±0.0	0.007	7.2±0.1	7.4±0.1	0.106
Total cholesterol, mg/dL	193.2±0.7	196.6±2.3	0.148	191.0±2.3	192.1±4.0	0.806
Triglycerides, mg/dL[b]	112.1 (109.0–115.2)	121.5 (112.2–131.5)	0.059	146.1 (137.4–155.5)	147 (127.9–168.8)	0.941
BUN, mg/dL	14.1±0.1	14.9±0.2	0.006	15.6±0.3	16.7±0.5	0.063
Creatinine, mg/dL	0.8±0.0	0.8±0.0	0.882	0.9±0.0	0.9±0.0	0.854
GFR, mL/min/1.73 m^2	92.8±0.5	92.4±1.2	0.706	87±1.1	88.5±2.2	0.551
ACR, mg/g[b]	4.2 (4.0–4.4)	75.8 (67.7–84.9)	<0.001	6.6 (5.8–7.4)	116.9 (92.9–147.1)	<0.001
Duration of DM, yr	-	-	-	4.8±0.4	6.1±0.6	0.084
New onset DM[a]	-	-	-	37.6 (2.9)	36.6 (4.4)	0.851
HTN[a]	24.5 (0.9)	48.8 (3.3)	<0.001	53.4 (2.9)	64.8 (5.1)	0.066
Medication for HTN[a]	13.0 (0.7)	27.5 (2.8)	<0.001	43.9 (2.5)	48.7 (5.4)	0.419
Dyslipidemia[a]	21.9 (0.8)	25.7 (2.9)	0.179	44.9 (2.9)	47.3 (4.4)	0.657
Medication for dyslipidemia[a]	3.6 (0.3)	3.5 (0.8)	0.855	19.1 (2.3)	13.3 (2.9)	0.142
CVD[a]	2.3 (0.3)	3.5 (0.9)	0.148	6.7 (1.2)	9.8 (2.7)	0.281
Alcohol consumption[a]	11.6 (0.7)	12.7 (2.1)	0.571	10.5 (1.8)	16.1 (4.0)	0.190
Smoking[a]	23.9 (1.0)	25.1 (2.8)	0.700	27.4 (2.6)	28.5 (3.7)	0.809
Exercise[a]	20.6 (0.9)	20.4 (2.7)	0.957	16.4 (2.2)	17.4 (3.6)	0.790

Values are presented as mean±standard error. BMI was defined as body mass (kg) divided by the square of height (m^2).
BMI, body mass index; WC, waist circumference; SBP, systolic blood pressure; FPG, fasting plasma glucose; HbA1c, hemoglobin A1c; BUN, blood urea nitrogen; GFR, glomerular filtration rate; ACR, albumin creatinine ratio; DM, diabetes mellitus; HTN, hypertension; CVD, cardiovascular disease.
[a]Values are presented as % (standard error), [b]ACR and triglyceride levels are presented as geometric mean (95% confidence interval).

Association between glucose tolerance categories and CKD

In the logistic regression analysis to determine the impact of diabetes on CKD, subjects with diabetes had an increased risk of CKD compared to those without diabetes (OR, 1.83; 95% CI, 1.13 to 2.96; *P*<0.0001) after adjusting for age, sex, BMI, SBP, exercise status, smoking status, and alcohol consumption status. When we categorized the subjects into three groups according to glucose tolerance status and diabetes duration (normal, IFG, and diabetes), IFG and diabetes were significant risk factors for CKD after adjusting for age, sex, BMI, SBP, exercise status, smoking status, and alcohol consumption status (Table 7).

DISCUSSION

In this study, using the dataset from KNHANES, we demonstrated that the prevalences of microalbuminuria, macroalbuminuria, and CKD were 22.0%, 4.7%, and 8.6%, respectively, in Korean subjects with diabetes, which were significantly higher than in those without diabetes. In subjects with diabetes, only blood pressure was significantly associated with albuminuria, while older age, higher serum triglyceride levels, and previous CVD events were the determinants of CKD.

In the United States, a study using data from the Third Na-

Table 3. Determinants of albuminuria according to diabetes status

	No diabetes		Diabetes	
	OR (95% CI)	*P* value	OR (95% CI)	*P* value
Age	1.01 (1.00–1.02)	0.190	1.01 (0.99–1.04)	0.273
Male sex	0.73 (0.47–1.13)	0.157	1.31 (0.77–2.22)	0.320
BMI	1.05 (1.00–1.10)	0.042	0.97 (0.91–1.04)	0.450
SBP	1.03 (1.02–1.04)	<0.001	1.03 (1.02–1.04)	<0.001
HbA1c	1.20 (0.76–1.90)	0.438	1.18 (0.99–1.39)	0.059
Total cholesterol[a]	0.99 (0.96–1.03)	0.768	1.00 (0.94–1.06)	0.972
Triglycerides[a]	1.00 (0.99–1.01)	0.814	1.01 (0.99–1.03)	0.391
Creatinine	0.93 (0.31–2.76)	0.895	0.82 (0.34–1.96)	0.655
Alcohol	1.02 (0.70–1.50)	0.912	1.23 (0.58–2.61)	0.588
Smoking	1.33 (0.88–2.00)	0.179	1.02 (0.55–1.88)	0.959

OR, odds ratio; CI, confidence interval; BMI, body mass index; SBP, systolic blood pressure; HbA1c, hemoglobin A1c.
[a]ORs are expressed per 10 mg/dL difference in total cholesterol and triglyceride concentrations.

Table 4. Odds ratio for albuminuria according to the glucose tolerance categories

	Model 1	Model 2	Model 3
No diabetes	Reference	Reference	Reference
IFG	1.45 (1.05–2.01)	1.22 (0.89–1.67)	1.20 (0.87–1.65)
New onset DM	3.11 (2.10–4.60)	2.55 (1.71–3.81)	2.53 (1.69–3.80)
Known DM	2.84 (2.03–3.97)	2.50 (1.76–3.42)	2.44 (1.75–3.41)
P for trend	<0.001	<0.001	<0.001

Values are presented as the odds ratio (95% confidence interval). Model 1: adjusted for age and sex; Model 2: adjusted for age, sex, body mass index (BMI), and systolic blood pressure (SBP); Model 3: adjusted for age, sex, BMI, SBP, exercise, drinking, and smoking.
IFG, impaired fasting glucose; DM, diabetes mellitus.

tional Health and Nutrition Examination Survey (NHANES III), which was conducted between 1988 and 1994, reported that the prevalence of microalbuminuria and macroalbuminuria was 35% and 6%, respectively, in adults with type 2 diabetes aged ≥40 years [19]. In 930 subjects with diabetes in the Shanghai Diabetic Complications Study, the prevalence of microalbuminuria was 22.8% and that of macroalbuminuria was 3.4% [20], which were similar to those in the present study. Few studies have evaluated the epidemiology of albuminuria in Korea. The prevalence of albuminuria was 34% (20%, microalbuminuria; 14%, macroalbuminuria) in 631 Korean patients with type 2 diabetes in a single hospital in 1995 [11], and

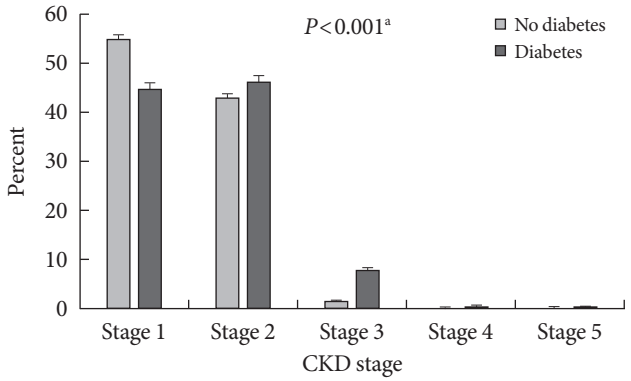

Fig. 3. Distribution of chronic kidney disease (CKD) stage according to diabetes status. [a]*P* value for the comparison of the proportion of subjects with CKD, compared between subjects with and without diabetes.

the duration of diabetes was longer than that in the present study. In a multicenter study conducted in a primary care setting, albuminuria was present in 29.4% (23.1%, microalbuminuria; 6.3%, macroalbuminuria) of 3,738 patients with type 2 diabetes and hypertension [16]. Because these two studies were conducted in a hospital or primary care clinic, the prevalence of albuminuria was higher than that in the present study. We believe the present study to be the first to report the prevalence of albuminuria using a nationally representative dataset in Korea, given the use of data from KHANES V, which was the first survey to measure albuminuria.

Diabetes is considered to be a key risk factor for albuminuria. We also report here that diabetes was associated with an approximate 2.5-fold increased risk of albuminuria. There have been few previous studies investigating the association between prediabetes and albuminuria [21,22]. In our study, IFG was associated with an increased risk of albuminuria after adjusting for age and sex; however, the association was no longer significant after further adjustment for BMI and SBP, which are important risk factors for albuminuria. In a population-based cross-sectional study conducted with 1,791 Korean subjects aged >40 years in the Jungup district, the prevalence of microalbuminuria was higher in subjects with prediabetes than in those with normal glucose tolerance (11.8% vs. 6.0%, *P*<0.0001), and this relationship was consistent even in hypertensive individuals [23]. However, the authors did not adjust for other potential confounding factors for albuminuria.

In our study, only SBP was an independent risk factor for albuminuria in subjects with diabetes. However, BMI was a significant risk factor for albuminuria in subjects without diabetes

Table 5. Clinical characteristics of the study population according to chronic kidney disease and diabetes diagnoses

	No diabetes			Diabetes		
	No CKD (n=18,642)	CKD (n=443)	P value	No CKD (n=2,185)	CKD (n=251)	P value
Age, yr	48.2±0.2	69.6±0.7	<0.001	57.8±0.3	68.4±0.8	<0.001
Male sex[a]	48.4 (0.3)	46.5 (2.8)	0.500	55.9 (1.2)	48.1 (3.7)	0.046
BMI, kg/m^2	23.7±0.0	24.1±0.2	0.082	25.1±0.1	25.2±0.3	0.670
WC, cm	81.4±0.1	84.7±0.5	<0.001	87.4±0.3	88.2±0.7	0.293
SBP, mm Hg	118.4±0.2	131.7±1.3	<0.001	127.3±0.5	131.2±1.4	0.008
FPG, mg/dL	93.4±0.1	96.4±0.6	<0.001	145.8±1.2	135.2±4.1	0.014
HbA1c, %	-	-	-	7.4±0.0	7.4±0.1	0.716
Total cholesterol, mg/dL	191±0.3	191.2±2.2	0.935	191.1±1.1	182.2±3.1	0.007
Triglyceride, mg/dL[b]	111.7 (110.4–113.0)	131.5 (124.7–138.5)	<0.001	149.6 (144.7–154.7)	155.3(143–168.7)	0.404
BUN, mg/dL	14.2±0.0	21.8±0.7	<0.001	15.3±0.1	23.3±0.7	<0.001
Creatinine, mg/dL	0.8±0.0	1.4±0.1	<0.001	0.8±0	1.5±0.1	<0.001
GFR, mL/min/1.73 m^2	93.8±0.3	51.5±0.6	<0.001	91.2±0.5	48.1±1	<0.001
Duration of DM, yr	-	-	-	5.1±0.2	10.7±0.7	<0.001
Medication for DM[a]	-	-	-	60.7 (1.3)	85.2 (2.5)	<0.001
HTN[a]	28.0 (0.5)	71.3 (2.6)	<0.001	55.6 (1.3)	83.8 (2.5)	<0.001
Medication for HTN[a]	13.5 (0.3)	61.1 (2.8)	<0.001	42.6 (1.3)	77.8 (2.9)	<0.001
Dyslipidemia[a]	20.7 (0.4)	33.0 (2.5)	<0.001	39.9 (1.3)	46.0 (3.6)	0.107
Medication for dyslipidemia[a]	3.0 (0.1)	7.7 (1.4)	<0.001	14.2 (0.9)	25.3 (3.6)	<0.001
CVD[a]	2.1 (0.1)	14.7 (2.0)	<0.001	6.8 (0.6)	17.9 (2.7)	<0.001
Alcohol consumption[a]	10.5 (0.3)	3.2 (0.9)	<0.001	12.6 (1.0)	3.0 (1.3)	<0.001
Smoking[a]	24.7 (0.4)	12.3 (1.9)	<0.001	25.3 (1.2)	15.3 (3.0)	0.007
Exercise[a]	23.8 (0.4)	15.0 (2.0)	<0.001	22.7 (1.1)	11.7 (2.1)	<0.001

Values are presented as mean±standard error. BMI was defined as body mass (kg) divided by the square of height (m^2).
CKD, chronic kidney disease; BMI, body mass index; WC, waist circumference; SBP, systolic blood pressure; FPG, fasting plasma glucose; HbA1c, hemoglobin A1c; BUN, blood urea nitrogen; GFR, glomerular filtration rate; DM, diabetes mellitus; HTN, hypertension; CVD, cardiovascular disease.
[a]Values are presented as % (standard error), [b]Triglyceride levels are presented as geometric mean (95% confidence interval).

but not in those with diabetes. The positive association between BMI or WC and albuminuria has been reported in previous epidemiological studies [24,25]. In patients with diabetes in the Look AHEAD (Action for Health in Diabetes) Study, higher BMI and abdominal obesity (determined using WC) were found to be associated with albuminuria [26], where the majority of participants had a BMI ≥30 kg/m^2. However, there has been some debate in this topic relating to subjects with diabetes. Lee et al. [27] reported that metabolic syndrome was an independent risk factor for albuminuria in 642 nonhypertensive Korean subjects with type 2 diabetes. However, of the various components of metabolic syndrome, abdominal obesity was not significantly related to microalbuminuria. Wentworth et al. [28] also reported that, in people with type 2 diabetes, there was a weaker correlation between BMI and albuminuria than in those without diabetes. We are not currently aware of the mechanism for this finding. BMI can be affected by diabetes treatment, the degree of hyperglycemia, and the insulin secretory capacity in diabetes. Therefore, the association between albuminuria and BMI could be attenuated by the diverse pathophysiology related to obesity in subjects with diabetes. Furthermore, the lower BMI values observed in the present study, than that in studies on Caucasians, may be responsible for the lack of association between albuminuria and BMI.

Compared to previous studies with Korean patients with diabetes, which reported that male sex, poor glycemic control, high blood pressure, diabetes duration, presence of diabetic retinopathy, homocysteine levels, BMI, and fasting insulin lev-

Table 6. Determinants of chronic kidney disease according to diabetes status

	No diabetes		Diabetes	
	OR (95% CI)	*P* value	OR (95% CI)	*P* value
Age	1.11 (1.10–1.13)	<0.001	1.08 (1.06–1.10)	<0.001
Female sex	1.19 (0.90–1.57)	0.225	1.26 (0.86–1.82)	0.238
WC	1.02 (1.01–1.04)	0.002	1.02 (1.00–1.03)	0.114
SBP	1.01 (1.00–1.02)	0.054	1.00 (0.99–1.01)	0.681
FPG[a]	1.04 (0.91–1.12)	0.577	0.97 (0.92–1.02)	0.233
Triglycerides[a]	1.02 (1.01–1.02)	<0.001	1.01 (1.00–1.03)	0.014
Total cholesterol[a]	0.97 (0.93–1.01)	0.132	0.94 (0.90–0.98)	0.004
CVD	2.40 (1.65–3.48)	<0.001	1.53 (0.99–2.36)	0.056
DM duration	-	-	1.06 (1.04–1.08)	<0.001
Alcohol consumption	0.41 (0.22–0.78)	0.007	0.39 (0.16–0.95)	0.039
Smoking	0.70 (0.47–1.03)	0.070	0.74 (0.43–1.29)	0.284
Exercise	0.77 (0.55–1.07)	0.114	0.56 (0.36–0.86)	0.009

OR, odds ratio; CI, confidence interval; WC, waist circumference; SBP, systolic blood pressure; FPG, fasting plasma glucose; CVD, cardiovascular disease; DM, diabetes mellitus.
[a]ORs are expressed per 10 mg/dL difference in FPG, triglycerides, and total cholesterol.

Table 7. Odds ratio for chronic kidney disease according to the glucose tolerance categories

	Model 1	Model 2	Model 3
No diabetes	Reference	Reference	Reference
IFG	1.93 (1.37–2.72)	1.67 (1.17–2.38)	1.72 (1.21–2.47)
DM	2.74 (1.75–4.31)	2.19 (1.31–3.67)	2.13 (1.29–3.53)
P for trend	<0.001	<0.001	<0.001

Values are presented as the odds ratio (95% confidence interval). Model 1: adjusted for age and sex; Model 2: adjusted for age, sex, body mass index (BMI), and systolic blood pressure (SBP); Model 3: adjusted for age, sex, BMI, SBP, exercise, drinking, and smoking.
IFG, impaired fasting glucose; DM, diabetes mellitus.

el were associated with an increased risk of microalbuminuria [11-16], blood pressure was the only significant variable in the present study, and HbA1c was only a marginally significant determinant. To clarify the causal relationship between these variables, future longitudinal studies in this population are warranted.

According to the present study conducted in Korea, the prevalence of CKD in subjects with diabetes was 8.6%, lower than in Western populations as well as other East Asian populations [29]. In the United States, the prevalence of CKD increased from 14.9% in NHANES 1988–1994 to 17.7% in NHANES 2005–2008 in patients with diabetes [30]. The prevalence of CKD in patients with type 2 diabetes in Asia was 10.2% in China [31] and 15.3% in Japan [32]. The differences between the two countries might be explained by the different ethnicities and MDRD equations. Following calculation of eGFR in the present study using the different MDRD equations, the prevalence of CKD was 6.8% using the Chinese equation [31] and 38.5% using the Japanese equation [32]. When Kang et al. [17] defined CKD as GFR <60 mL/min/1.73 m^2 or proteinuria as ≥1+ using KNHANES IV, which was used in the present study, the prevalence of CKD was 4.5% in men and 6.3% in women among subjects with or without diabetes. However, they did not compare the prevalence of CKD by diabetes status. Therefore, this is the first study to ascertain the status of CKD in Korean subjects with diabetes on a national scale.

In this study, older age, higher serum triglyceride levels, and longer diabetes duration were associated with an increased risk of CKD, whereas serum total cholesterol level, heavy alcohol drinking, and exercise were associated with a decreased risk of CKD in patients with diabetes. High serum triglyceride levels are considered a risk factor for diabetic nephropathy [33], and this was also true in our study. CKD induces hypertriglyceridemia through impaired clearance of triglyceride-rich lipoproteins [34]. However, we found a negative association between serum cholesterol and CKD, contrary to the findings of previous studies. The reason for this discrepancy is unknown. However, higher doses of lipid lowering medication may be responsible for the lower cholesterol levels in subjects with diabetes and CKD than that in those without CKD. In the previous study using KNHANES data, regular drinking (alcohol consumption ≥1/wk) may have been partly associated with the reduced rates of CKD in men, which is consistent with our study [17]. However, there have been reports that alcohol consumption could be a risk factor for diabetic nephropathy. In the AusDiab study, moderate-to-high alcohol consumption contributed to the development of albuminuria [22]. Subjects with diabetes and CKD in the present study may have led a healthier lifestyle, as evidenced by lower blood glucose and lipid levels, a greater use of medications for diabetes or dyslipidemia, and fewer smokers, although they exercised less. Therefore, the independent relationship between alcohol and CKD may be confounded by the awareness of the diabetes status in subjects with CKD, which led to a better lifestyle.

Our study has some limitations. The cross-sectional design limits inferences about causality. Second, we could not exclude patients with conditions that could elevate urinary albumin excretion, such as hematuria, pregnancy, urinary tract infection, or other febrile illness, and we could not repeat the random urine sampling for the determination of albuminuria. Instead, the ACR measurement was based on a single random urine sample, not the first morning voided urine. Moreover, the epidemiology of diabetic nephropathy in type 1 diabetes differs from that of type 2 diabetes [35]; however, we could not determine the type of diabetes in our study. Last, we used the KNHANES IV–V dataset from 2008 to 2011 for the assessment of CKD prevalence to obtain a sufficient number of subjects with diabetes and CKD. However, HbA1c was not measured in all participants in KNHANES from 2007 to 2010; therefore, the prevalence of diabetes could be underestimated. Despite these potential limitations, this study has several strengths; for example, the data were based on a nationally representative population, and we adjusted for multiple risk factors in order to evaluate the determinants of diabetic nephropathy.

In conclusion, Korean subjects with diabetes had a higher prevalence of albuminuria and CKD than those without diabetes. In subjects with diabetes, blood pressure was significantly associated with an increased risk of albuminuria, and older age, higher serum triglyceride levels, and a longer diabetes duration were determinants of CKD. To investigate the causal relationship between the risk factors and the development of albuminuria and CKD, future longitudinal follow-up studies are warranted.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

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