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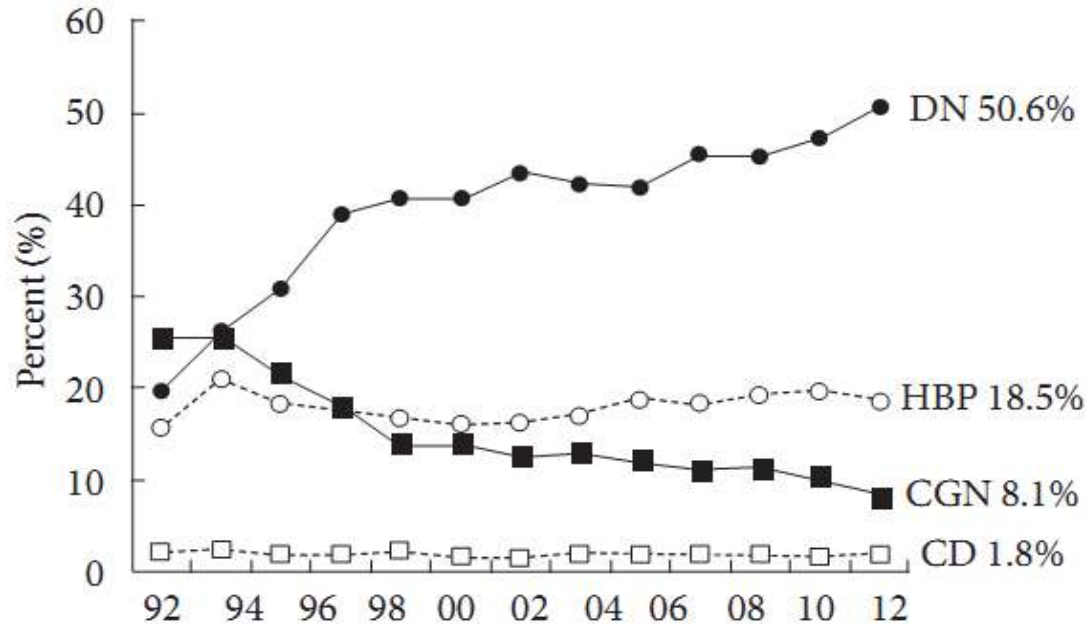
; Korea National Health and Nutrition Examination Survey

Division of Endocrinology and Metabolism, Department of Internal Medicine, College of Medicine, Korea University
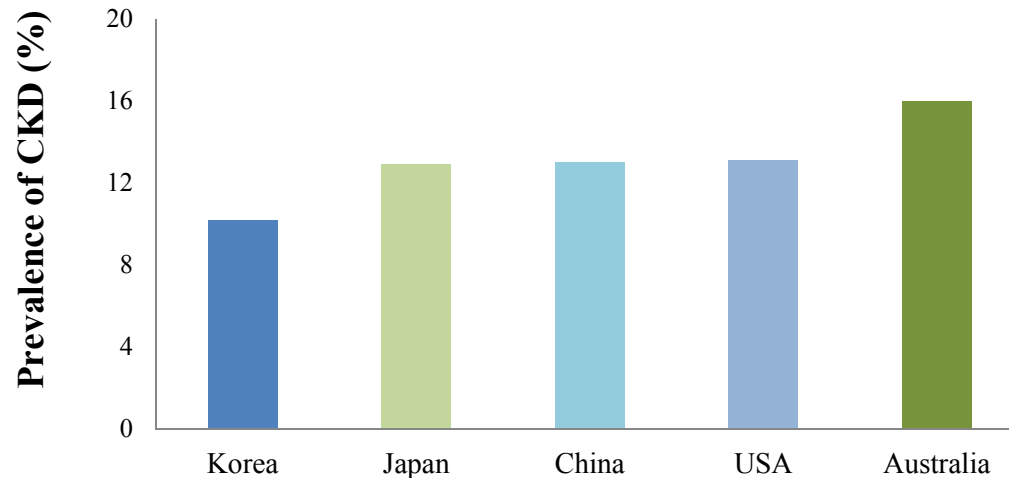
JH Ahn, MD.

Diabetic Nephropathy (DN)

• **Diabetic nephropathy**

- **leading cause of ESRD (end-stage renal disease) in Korea**

- **associated with increased cardiovascular mortality**

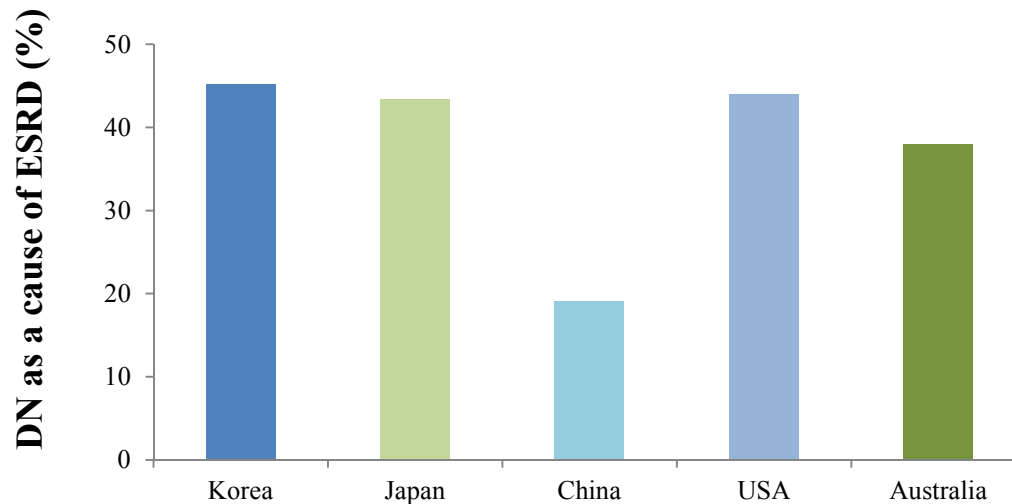The causes of ESRD patients who were initiated renal replacement therapy in each year in Korea

Ethnic diversity of diabetic nephopathy

The prevalence of chronic kidney disease in adult population in 2008

The proportaion of DN as a cause of ESRD in 2011

Diabetes Metab J 2014;38:252-260
Nephrol Dial Transplant 2010;25: 413–419
Clin Exp Nephrol 2009;13:621-30.
Am J Kidney Dis 2008;51:373-84.

Previous studies in Korea

First author	Year	Sample	Study design	Albuminuria	Reference
Lee at al.	1995	631 with T2DM	Cross sectional Single center	20% had microalbuminuria, 14% had overt proteinuria	Diabetes Care. 1995 Jun;18(6):793-9
Park et al.	1998	146 with new T2DM	Longitudinal Single center	The incidence of microalbuminuria was 51.6/1000 person-years	Diabetes Care. 1998 Apr;21(4):530-4.
Kim at al.	2006	5,915 with T2DM	Cross sectional Single center	7.7 % had microalbuminuria	Korean J Med. 2006;70:617–626.
Kim at al.	2007	304 with new T2DM	Cross sectional Single center	17 % had microalbuminruia	Korean J Med. 2007;73:503–511

Therefore, the study for the prevalence of diabetic nephropathy and its determinants was needed at the national level in Korea.

Objectives

- Korean National Health and Nutrition Examination Survey (KNHANES)

- To determine the prevalence and determinants of albuminuria and chronic kidney disease (CKD) according to the status of diabetes

- To determine the impact of prediabetes and diabetes on albuminuria and CKD

Methods

Method

- **Cross sectional study**

- **Study population**
  - Age $\geq$ 30 years
  - Albuminuria (n = 4,652) : dataset from KNHANES V
  - CKD (n = 21,521) : dataset from KNHANES IV – V

Diabetic nephropathy

- **Diabetic nephropathy**
  - Presence of albuminuria or decreased eGFR

- **Albuminuria**
  - Spot urine albumin/creatinine ratio (ACR)
  - Albuminuria: ACR $\geq$ 30 mg/g
    - Microalbuminruia : 30 mg/g $\leq$ ACR < 300mg/g
    - Macroalbuminuria : 300mg/g $\leq$ ACR

- **Chronic kidney disease (CKD)**
  - eGFR by MDRD formula
  - eGFR <60 mL/min/1.73m^2

Definition of diabetes and glucose categories

- **Diabetes**
  - New onset diabetes : FPG $\geq$ 126 mg/dL or HbA1c $\geq$ 6.5 %, first detected in our survey
  - Known diabetes

- **Impaired fasting glucose (IFG)**
  - 100 mg/dL $\leq$ FPG < 126 mg/dL

Results

Albuminuria

Clinical characteristics of study population

	No Diabetes (N=3992)	Diabetes (N=660)	P-value
Age (yr)	**49.2 ± 0.4**	**58.8 ± 0.7**	**<.001**
Male †	50.1 (0.8)	57.6 (2.1)	0.002
BMI (kg/m²)	**23.8 ± 0.1**	**25.2 ± 0.2**	**<.001**
WC (cm)	81.9 ± 0.2	87.9 ± 0.5	<.001
SBP (mmHg)	118.3 ± 0.4	127.1 ± 1.0	<.001
FPG (mg/dL)	92.8 ± 0.2	138.0 ± 2.1	<.001
HbA1c (%)	5.5 ± 0.0	7.3 ± 0.1	<.001
TC (mg/dL)	193.5 ± 0.7	191.3 ± 2.0	0.299
Tg* (mg/dL)	113.0 (110.1-116)	146.4 (138-155.3)	<.001
eGFR (ml/min)	**92.8 ± 0.4**	**87.4 ± 1**	**<.001**
ACR* (mg/g)	**5.7 (5.3-6.0)**	**14.1 (12.1-16.6)**	**<.001**
Duration of DM (yr)	.	**5.1 ± 0.3**	.
HTN †	**27.0 (0.9)**	**56.5 (2.5)**	**<.001**
Dyslipidema †	**22.3 (0.8)**	**45.6 (2.3)**	**<.001**
CVD †	2.4 (0.2)	7.6 (1.0)	<.001
Alcohol †	11.7 (0.7)	12.0 (1.6)	0.883
Smoking †	24.0 (0.9)	27.7 (2.1)	0.085
Exercise †	20.5 (0.8)	16.7 (2.0)	0.065

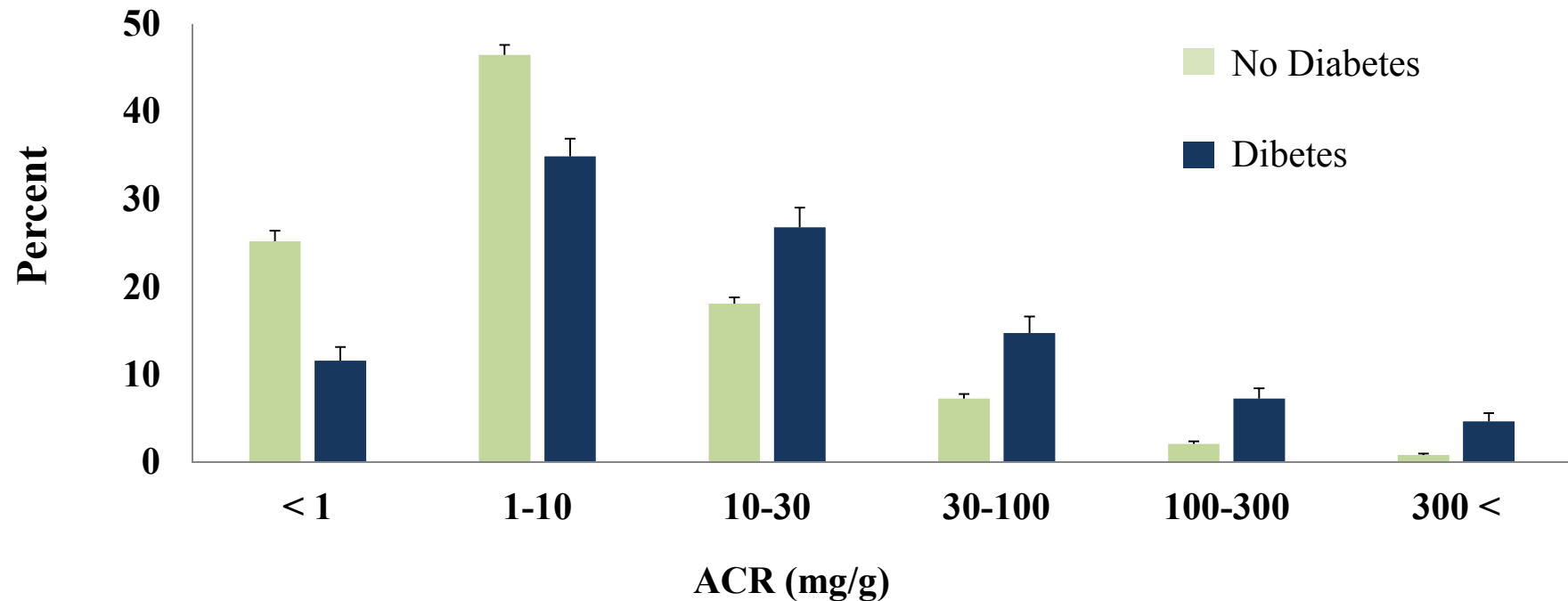Values are presented as mean ± standard error.

† Values are presented as % (standard error)

*ACR, Triglyceride levels are presented as geometric mean (95% confidence interval).

. WC, waist circumference; SBP, systolic blood pressure; FPG, fasting plasma glucose; TC, total choelsterol, Tg, Triglyceride, eGFR, estimated glomerular filtration rate; ACR, albumin creatinine ratio; DM, diabetes mellitus; CVD, cardiovascular disease.

Albuminuria

Distribution of albumin creatinine ratio according to the status of diabetes
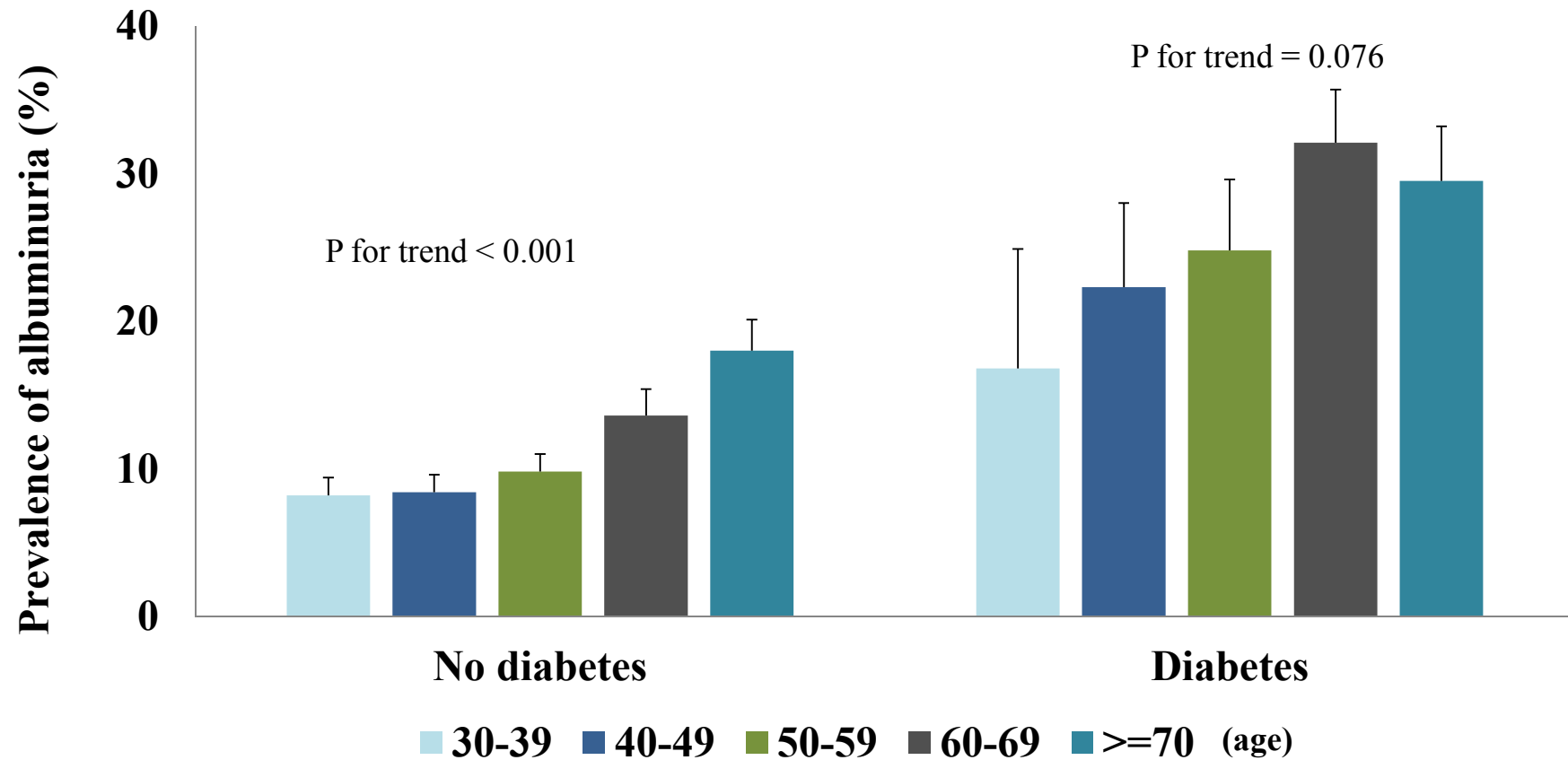
* Prevalence of albuminuria

	No diabetes	Diabetes
N	407/3992	135/660
%	10.2 %	26.7 %

Albuminuria

Prevalence of albuminuria according to the age and diabetes status

Odds ratio for albuminuria
according to the glucose tolerance categories

	Model 1	Model 2	Model 3
No Diabetes	*ref*	*ref*	*ref*
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	<.001	<.001	<.001

Values are presented as odds ratio with 95% confidence interval.

Model 1 : adjusted for age, sex
Model 2 : adjusted for age, sex, BMI, SBP
Model 3 : adjusted for age, sex, BMI, SBP, exercise, drinking, smoking

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

	No diabetes			Diabetes		
	Normal (N=3599)	Albuminuria (N=393)	P-value	Normal (N=480)	Albuminuria (N=180)	P-value
Age (yr)	48.9 ± 0.4	52.6 ± 1.0	<.001	58.1 ± 0.8	60.8 ± 1.2	0.064
BMI (kg/m²)	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	<.001	88.0 ± 0.5	87.6 ± 1	0.714
SBP (mmHg)	117.4 ± 0.4	126.1 ± 1.4	<.001	124.4 ± 0.9	134.7 ± 1.9	<.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
TC (mg/dL)	193.2 ± 0.7	196.6 ± 2.3	0.148	191.0 ± 2.3	192.1±4.0	0.806
Tg* (mg/dL)	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
eGFR (ml/min/1.73m²)	92.8 ± 0.5	92.4 ± 1.2	0.706	87 ± 1.1	88.5 ± 2.2	0.551
ACR* (mg/g)	4.2 (4.0-4.4)	75.8 (67.7-84.9)	<.001	6.6 (5.8-7.4)	116.9 (92.9-147.1)	<.001
Duration of DM (yr)				4.8 ± 0.4	6.1 ± 0.6	0.084
HTN †	24.5 (0.9)	48.8 (3.3)	<.001	53.4 (2.9)	64.8 (5.1)	0.066
Dyslipidema †	21.9 (0.8)	25.7 (2.9)	0.179	44.9 (2.9)	47.3 (4.4)	0.657
CVD †	2.3 (0.3)	3.5 (0.9)	0.148	6.7 (1.2)	9.8 (2.7)	0.281
Alchhol †	11.6 (0.7)	12.7 (2.1)	0.571	10.5 (1.8)	16.1 (4.0)	0.190
Smoking-†	23.9 (1.0)	25.1 (2.8)	0.700	27.4 (2.6)	28.5 (3.7)	0.809
Exercise †	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.

† Values are presented as % (standard error)

*ACR, Triglyceride levels are presented as geometric mean (95% confidence interval).

. WC, waist circumference; SBP, systolic blood pressure; FPG, fasting plasma glucose; TC, total choelsterol, Tg, Triglyceride, eGFR, estimated glomerular filtration rate; ACR, albumin creatinine ratio; DM, diabetes mellitus; CVD, cardiovascular disease.

Albuminuria

Determinants of albuminuria according to the status of diabetes

	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
Sex (male)	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*	0.99	(0.96-1.03)	0.768	1.00	(0.94-1.06)	0.972
Triglyceride*	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

Odds ratios were expressed for 10 mg/dL difference of total cholesterol and triglyceride.
Adjusted for age, sex, BMI, HbA1c, total cholesterol, triglyceride, creatinine, alcohol drinking and smoking status

Clinical characteristics of study population according to chronic kidney disease (CKD) and diabetes diagnosis

	Non DM			DM		
	No CKD (N=18642)	CKD (N=443)	P-value	No CKD (N=2185)	CKD (N=251)	P-value
Age (yr)	48.2 ± 0.2	69.6 ± 0.7	<.001	57.8 ± 0.3	68.4 ± 0.8	<.001
Male †	48.4 (0.3)	46.5 (2.8)	0.500	55.9 (1.2)	48.1 (3.7)	0.046
BMI (kg/m²)	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	<.001	87.4 ± 0.3	88.2 ± 0.7	0.293
SBP (mmHg)	118.4 ± 0.2	131.7 ± 1.3	<.001	127.3 ± 0.5	131.2 ± 1.4	0.008
FPG (mg/dL)	93.4 ± 0.1	96.4 ± 0.6	<.001	145.8 ± 1.2	135.2 ± 4.1	0.014
TC (mg/dL)	191 ± 0.3	191.2 ± 2.2	0.935	191.1 ± 1.1	182.2 ± 3.1	0.007
Tg* (mg/dL)	111.7 (110.4-113.0)	131.5 (124.7-138.5)	<.001	149.6 (144.7-154.7)	155.3 (143-168.7)	0.404
eGFR (ml/min/1.73m²)	93.8 ± 0.3	51.5 ± 0.6	<.001	91.2 ± 0.5	48.1 ± 1	<.001
Duration of DM (yr)				5.1 ± 0.2	10.7 ± 0.7	<.001
HTN †	28.0 (0.5)	71.3 (2.6)	<.001	55.6 (1.3)	83.8 (2.5)	<.001
Dyslipidema †	20.7 (0.4)	33.0 (2.5)	<.001	39.9 (1.3)	46.0 (3.6)	0.107
CVD †	2.1 (0.1)	14.7 (2.0)	<.001	6.8 (0.6)	17.9 (2.7)	<.001
Alcohol †	10.5 (0.3)	3.2 (0.9)	<.001	12.6 (1.0)	3.0 (1.3)	<.001
Smoking †	24.7 (0.4)	12.3 (1.9)	<.001	25.3 (1.2)	15.3 (3.0)	0.007
Exercise †	23.8 (0.4)	15.0 (2.0)	<.001	22.7 (1.1)	11.7 (2.1)	<.001

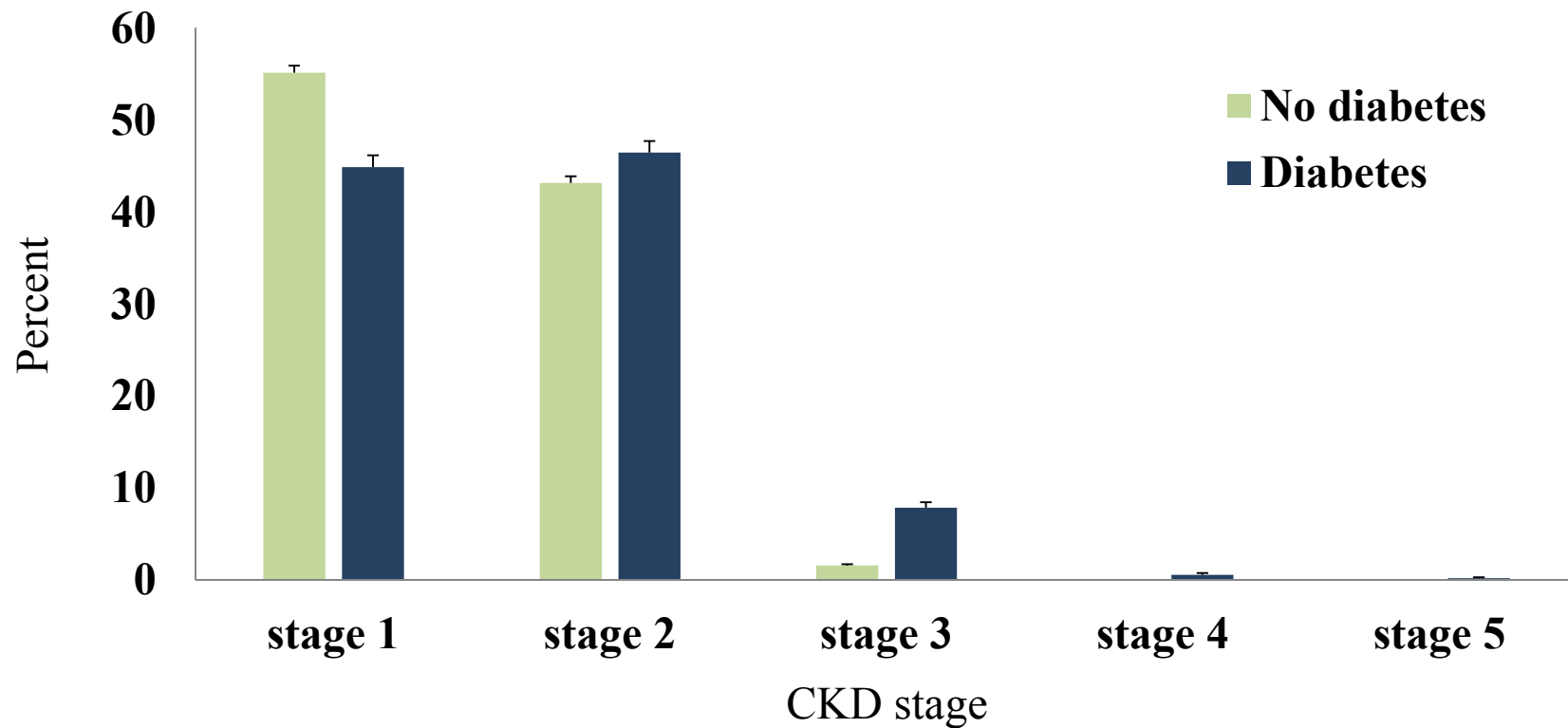Values are presented as mean ± standard error.

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. WC, waist circumference; SBP, systolic blood pressure; FPG, fasting plasma glucose; TC, total choelsterol, Tg, Triglyceride, eGFR, estimated glomerular filtration rate; ACR, albumin creatinine ratio; DM, diabetes mellitus; CVD, cardiovascular disease.

CKD

Distribution of CKD stage according to the status of diabetes

* Prevalence of CKD

	No diabetes	Diabetes
N	323/19085	215/2486
%	1.7 %	8.6 %

Odds ratio for CKD
according to the glucose tolerance categories

	Model 1	Model 2	Model 3
No Diabetes	*ref*	*ref*	*ref*
IFG	1.93 (1.37-2.72)	1.67 (1.17-2.38)	1.73 (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	<.001	<.001	<.001

Values are presented as odds ratio with 95% confidence interval.

Model 1 : adjusted for age, sex
Model 2 : adjusted for age, sex, BMI, SBP
Model 3 : adjusted for age, sex, BMI, SBP, exercise, drinking, smoking

Adjusted for age, sex, BMI, systolic blood pressure, exercise, smoking and alcohol drinking status

Determinants of CKD according to the status of diabetes

	No diabetes			Diabetes		
	OR	95% CI	P-value	OR	95% CI	P-value
Age	**1.11**	**(1.10-1.13)**	**<.001**	**1.08**	**(1.06-1.10)**	**<.001**
Sex(female)	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*	1.04	(0.91-1.12)	0.577	0.97	(0.92-1.02)	0.233
Triglyceride*	**1.02**	**(1.01-1.02)**	**<.001**	**1.01**	**(1.00-1.03)**	**0.014**
Total cholesterol*	**0.97**	**(0.93-1.01)**	**0.132**	**0.94**	**(0.90-0.98)**	**0.004**
CVD	2.40	(1.65-3.48)	<.001	1.53	(0.99-2.36)	0.056
DM duration				**1.06**	**(1.04-1.08)**	**<.001**
Alcohol	**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**

* Odds ratios were expressed for 10 mg/dL difference of FPG, triglyceride, and total cholesterol.

Conclusion

- Albuminuria and CKD are more prevalent in subjects with diabetes than those without

- IFG is independently associated with CKD, but not with albuminuria after adjusting for multiple risk factors

- In subjects with diabetes, increased blood pressure is major determinants of albuminuria

- The presence of CKD in diabetes is positively associated with age, triglyceride and duration of diabetes, and negatively with total cholesterol, alcohol consumption, and exercise

Thank you!