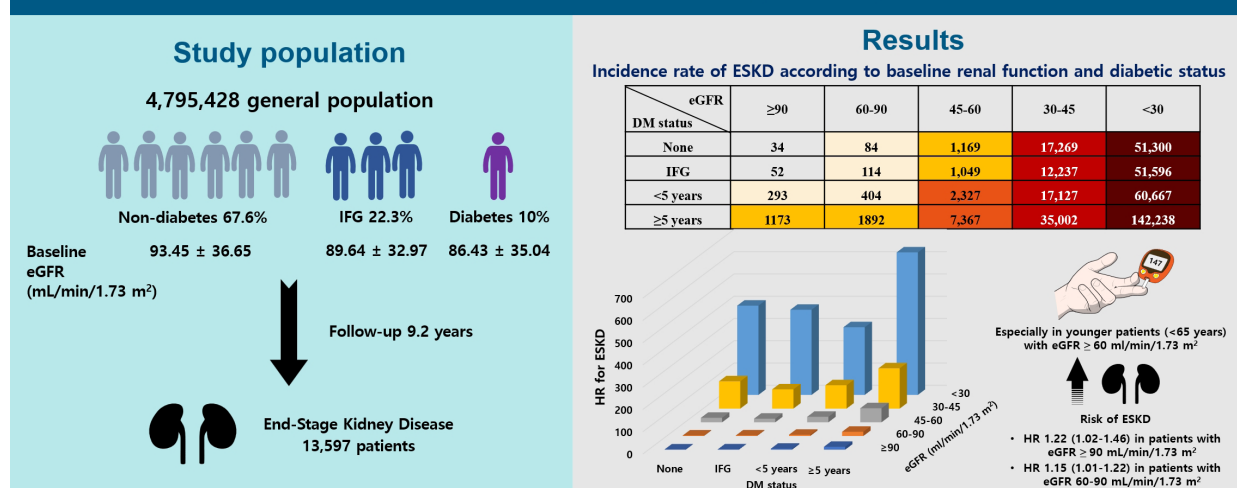


# Burden of End-Stage Kidney Disease by Type 2 Diabetes Mellitus Status in South Korea: A Nationwide Epidemiologic Study

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### Conclusion

Longer diabetes duration increases ESKD risk, even with normal renal function, while IFG elevates risk mainly in younger patients with early-stage CKD.



### Highlights

- In South Korea, ESKD incidence per million is 139 for nondiabetics and 188 for IFG.
- The rates are 632 for diabetics under 5 years and 3,430 for those over 5 years.
- Long-standing diabetes with normal kidney function raises ESKD risk 14-fold.
- IGF raises the risk of EKSD in younger individuals with early-stage CKD.

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# Burden of End-Stage Kidney Disease by Type 2 Diabetes Mellitus Status in South Korea: A Nationwide Epidemiologic Study

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**Background:** Patients with diabetes are known to be at high risk for end-stage kidney disease (ESKD), but the accurate annual risk data for new-onset ESKD is still limited. In South Korea, the prevalence and incidence of ESKD are increasing more rapidly compared to the global average. This study aimed to determine the incidence rate (IR) of ESKD by diabetes status from 2012 to 2022.

**Methods:** Using data from the Korean National Health Insurance Service, we calculated the IR and hazard ratio (HR) for new-onset ESKD in the general population. Individuals were categorized based on diabetes status into nondiabetes, impaired fasting glucose (IFG), diabetes duration <5 and ≥5 years.

**Results:** Among the participants, 67.6% were nondiabetic, 22.3% had IFG, and 10% had diabetes. In Korea, the IRs of ESKD were 139 per million population (pmp) for nondiabetes, 188 pmp for IFG, 632 pmp for diabetes <5 years, and 3,403 pmp for diabetes ≥5 years. An advanced estimated glomerular filtration rate (eGFR) category was the strongest risk factor for ESKD development. However, even in patients with normal renal function, those with long-standing diabetes had a 14-fold higher risk of ESKD compared to nondiabetic individuals. The risk of ESKD associated with diabetes increased exponentially with declining renal function. Notably, IFG showed an increasing tendency for ESKD in younger patients (<65 years) with early-stage chronic kidney disease (CKD; eGFR ≥60 mL/min/1.73 m<sup>2</sup>).

**Conclusion:** Longer diabetes duration amplifies ESKD risk, particularly as renal function declines. Even in patients with normal renal function, long-standing diabetes significantly increases ESKD risk, while IFG is associated with elevated risk only in younger individuals with early-stage CKD.


**Keywords:** Diabetes mellitus; Glucose intolerance; Incidence; Kidney failure, chronic; Korea

## INTRODUCTION

The global increase in the number of patients with end-stage kidney disease (ESKD) is a major public health challenge [1,2]. The prevalence of ESKD is estimated to be about 0.07%, and

approximately 5–10 million people worldwide suffer from ESKD [2]. The ESKD situation in South Korea is particularly grim, with the country leading the world in the rate of increase of ESKD patients [3,4]. According to the 2022 Annual Report using data from the United States Renal Data System, the high-

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est incidence of treated ESKD in 2020 was observed in Taiwan (525 per million population [pmp]), the United States (396 pmp), Singapore (366 pmp), the Republic of Korea (355 pmp), Thailand (339 pmp), Japan (307 pmp), and Indonesia (303 pmp) [5]. More importantly, the rate of increase of new ESKD patients is another significant issue in Korea. Korea ranks either first or second in the world in terms of the increasing rate of new ESKD patients [6,7]. On this basis, South Korea is one of the two countries where the average annual increase in dialysis prevalence will exceed 100.0 pmp between 2011 and 2021 (Thailand 124.2 pmp, South Korea 122.4 pmp).

Two major reasons for this rapid increase in Korea are diabetes and the aging of the population. First, more than half of all new ESKD cases in Korea are due to diabetes, with the increase in diabetic kidney disease (DKD) being the main driver of the increase in ESKD incidence. Despite improvements in glycemic control and blood pressure (BP) management with renin-angiotensin-aldosterone system blockade and sodium-glucose cotransporter-2 inhibitors, current therapy cannot completely halt the progression of DKD to ESKD in some patients [8,9]. In addition, DKD is a very heterogeneous disease entity with a wide range of clinical presentations [10,11]. For example, while it was previously thought that albuminuria preceded the decline in renal function in DKD, recent epidemiologic studies have identified a subset of DKD patients who experience renal dysfunction without developing albuminuria [12]. Furthermore, recent emphasis on screening for prediabetes highlights its association with macrovascular and microvascular complications due to insulin resistance and lipotoxicity from chronic or intermittent hyperglycemia [13,14]. Although diabetes-related renal complications have been well studied, there is still a paucity of data comparing long-term renal risks between patients with impaired fasting glucose (IFG) and those with diabetes.

Aging is another important factor in the rapid growth of new ESKD patients. By 2023, individuals aged 65 years and older accounted for 19% of South Korea's population, reflecting the country's transition to a 'super-aged society'. In fact, there is growing concern about a chronic kidney disease (CKD)/ESKD pandemic in the aging population [15]. Therefore, in elderly patients with diabetes, it is crucial to accurately assess the risk of renal progression based on each patient's individual condition and to make a long-term plan accordingly [16].

Under these circumstances, it's crucial to obtain accurate, up-to-date data that clearly and simply delineate the risk levels

of developing ESKD based on diabetes status in Korea in order to raise awareness of the seriousness of this issue. Using the Korean National Health Insurance Service (KNHIS) in South Korea, we addressed this issue in this study.

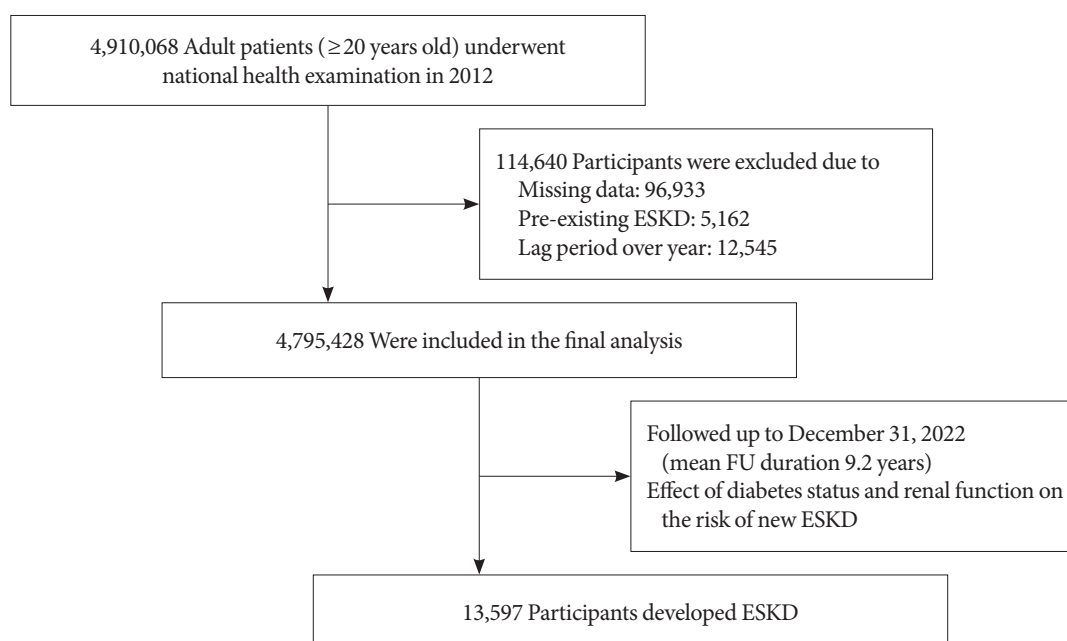
## METHODS

### KNHIS data

In this study, we used the national health insurance claims database established by the KNHIS, which includes all claims data provided by the KNHIS and Medical Aid programs. The KNHIS database is considered to represent the entire South Korean population, and the details of this database have been previously described. Depending on their occupations, all insured Koreans undergo an annual or biennial health examination that is supported by the KNHIS. The sociodemographic data and all medical expenses for both inpatient and outpatient services, pharmacy dispensing claims, and mortality information are included in the database. Anonymized data are publicly available from the NHIS database. This study was approved by the Institutional Review Board (IRB No. 2024-04-017) of Hallym University Sacred Heart Hospital and informed consent was waived. All data analysis was performed in accordance with the ethical standards of the committee responsible for human experimentation and the Helsinki Declaration.

### Subjects

Initially, 4,910,068 patients were identified who underwent a health examination in 2012. Of these, we excluded those aged <20 years because the development of ESKD is rare in this subpopulation. We also excluded subjects with a history of ESKD before the index date and those with missing health examination data. ESKD incidence was examined between 2013 and 2022. Finally, 4,795,428 subjects were included in the study (Fig. 1). Duration of diabetes was also available from the KNHIS database. It was defined as the period from the first prescription of diabetes medication, which could be confirmed from the claim records starting on January 1, 2002, to the date of the health examination in 2012. For risk stratification, we divided patients by the diabetes status, baseline renal function, and age. Diabetes status was divided into four groups: none, IFG, diabetes duration <5 years, and duration ≥5 years. Age was divided into three groups: <40, 40–65, and ≥65 years. The participants were followed up until one of the following occurred: a new diagnosis of ESKD, death, or the end of the study (December 31, 2022).



**Fig. 1.** Flow chart of the selection of study subjects. ESKD, end-stage kidney disease; FU, follow-up.

Case of death was censored in the analysis.

# Definitions

Patients with diabetes were defined as: (1) having at least one claim per year for a prescription of antidiabetic medication according to International Statistical Classification of Diseases, 10th Revision (ICD-10) codes E11 through E14 from insurance claims data, or (2) having a fasting plasma glucose level  $\geq 126$  mg/dL at the health examination without a prescription of antidiabetic medication. IFG was defined as fasting plasma glucose  $\geq 100$  but  $< 126$  mg/dL. Comorbidities were defined using ICD-10 diagnosis codes with healthcare utilization and medication or health assessment results, as in the previous studies. CKD stages were classified as 1, 2, 3a, 3b, and 4 if the estimated glomerular filtration rate (eGFR) was  $\geq 90$ , 60–90, 45–60, 30–45, and  $< 30$  mL/min/1.73 m<sup>2</sup> according to the CKD Modification of Diet in Renal Disease equation. Proteinuria was measured by a dipstick test. Low income was defined as the lowest 25% of socioeconomic status. The presence of dyslipidemia was defined according to the presence of at least one claim per year for the prescription of antihyperlipidemic agents under ICD-10 codes E78, or total cholesterol  $\geq 240$  mg/dL. Body mass index (BMI) was calculated as weight (in kilograms) divided by height (in meters squared). Smoking history was categorized as never, former, or current smoker. Alcohol

consumption was categorized as none, light, or heavy drinker ( $\geq 30$  g of alcohol per day). Regular exercise was defined as mid-term exercise  $\geq 5$  days or vigorous exercise  $\geq 3$  days in a week.

# Outcomes

Outcome data was retrieved between 2013 to 2022. The endpoint was incident ESKD, which was defined by a special code ('V001,' 'V003,' and 'V005') assigned for initiation of renal replacement therapy (hemodialysis [HD], V001; peritoneal dialysis [PD], V003) or kidney transplantation (V005). All medical expenses for dialysis are reimbursed through the Korean Health Insurance Review and Assessment Service database. These patients are also registered as special medical aid beneficiaries. Therefore, we were able to identify every patient with ESKD in the entire South Korean population and analyze data for all patients with ESKD who underwent dialysis. Subjects on continuous renal replacement therapy or acute PD were excluded.

# Statistical analyses

Data are presented as the mean  $\pm$  standard deviation for continuous variables and numbers with proportions for categorical variables. Nonnormally distributed variables are presented as geometric means (95% confidence interval [CI]). Intergroup differences were tested using a chi-square test or analysis of

variance (ANOVA), as appropriate. The incidence rate (IR) of ESKD are presented per 1,000 person-years. Multivariable Cox proportional hazard regression analysis was employed to estimate the hazard ratio (HR) and 95% CIs for the risk of ESKD associated with diabetes status and baseline renal function. The analysis adjusted for age, sex, income, smoking, drinking, exercise, hypertension, dyslipidemia, BMI, and proteinuria. In addition, to find the difference of HR by age, subgroup analysis was performed in two age groups: <65 and ≥65 years groups. All data analyses were conducted using SAS software version 9.4 (SAS Institute, Cary, NC, USA), and  $P < 0.05$  was considered statistically significant.

## RESULTS

### Baseline characteristics

Of the participants, 67.6% were nondiabetes, 22.3% had IFG, and 10% had diabetes. The characteristics of the participants, stratified according to diabetes status and duration, are compared in Table 1. Mean age was 45.7, 50.7, 55.8, and 62.5 years in patients with nondiabetic, IFG, DM duration <5 years, and ≥5 years, respectively. When age was divided into three groups, the percentage of participants aged ≥65 years increased significantly with increasing diabetes duration. Among patients with diabetes duration ≥5 years, about 42.7% ( $n=86,877$ ) were age ≥65 years, whereas only 1.3% ( $n=2,567$ ) were age <40 years.

As expected, most patients without diabetes were non-smokers (62.6%), were not heavy drinkers (93.8%), and had normal BP. Compared with individuals without diabetes, IFG patients were more likely to be smokers and alcohol drinkers, and had increased waist circumference, BP, and pulse pressure. The prevalence of hypertension and dyslipidemia was also significantly higher in the IFG group than in the nondiabetes group, suggesting significant differences in metabolic profiles between nondiabetes and IFG patients. Accordingly, individuals with IFG had a significantly lower eGFR (93.4 mL/min/1.73 m<sup>2</sup> vs. 89.6 mL/min/1.73 m<sup>2</sup>) but a higher prevalence of proteinuria (1.5% vs. 2.1%) compared to those without diabetes. Lipid profiles were also worse in the IFG group.

In patients with diabetes, these changes in the metabolic profile were more pronounced. Patients with diabetes duration ≥5 years had the highest rates of hypertension and dyslipidemia, as well as elevated systolic BP and pulse pressure. Interestingly, the prevalence of current smoking and heavy alcohol consumption was slightly lower in this group with diabetes du-

ration ≥5 years compared to patients with diabetes duration <5 years. The number of patients who exercised regularly was also higher in this group, indicating lifestyle modification in patients with longer duration of diabetes compared with patients with shorter duration of diabetes. Laboratory measurements showed that baseline eGFR decreased with increasing duration of diabetes. Among patients with ≥5 years of diabetes, approximately one in seven (14.4%) had CKD stage 3 or higher.

### Diabetes status and risk of ESKD by baseline renal function

During a mean follow-up of  $9.2 \pm 1.1$  years, 13,597 participants were diagnosed with ESKD. The IR of ESKD by diabetes status were 139, 188, 632, and 3,403 pmp in nondiabetes, IFG, DM duration <5 years, and ≥5 years, respectively. The HR and IR of ESKD by diabetes status and baseline renal function are summarized in Tables 2 and 3, using patients without diabetes and having normal renal function as a reference.

As expected, baseline eGFR was an important determinant of ESKD development. Patients with eGFR <45 mL/min/1.73 m<sup>2</sup> had a more than 100-fold increased risk of ESKD, regardless of diabetes status. Patients without diabetes and eGFR 45 to 60 had an even higher risk than those with DM duration ≥5 years but eGFR ≥90 mL/min/1.73 m<sup>2</sup> (HR 20.1 vs. 13.9). However, the presence of diabetes significantly influenced this progression to ESKD. Even among patients with normal renal function, those with long-standing diabetes had a 14-fold higher risk of ESKD compared to nondiabetic individuals (HR, 13.9; 95% CI, 12.4 to 15.7).

We further investigated the role of IFG in the development of ESKD across different eGFR categories. Our findings indicated a trend of increasing ESKD risk associated with IFG in patients with eGFR ≥60 mL/min/1.73 m<sup>2</sup>. While not statistically significant, the HR for IFG and new ESKD was 1.2 (95% CI, 0.99 to 1.4) in patients with eGFR ≥90 mL/min/1.73 m<sup>2</sup> and 1.09 (95% CI, 0.99 to 1.19) in those with eGFR 60–90 mL/min/1.73 m<sup>2</sup>, using nondiabetic individuals as the reference group. However, no association was observed between IFG and ESKD risk in patients with eGFR <60 mL/min/1.73 m<sup>2</sup>.

### Effect of age on the association between diabetes status and incident ESKD

We also examined the role of age in the diabetes-associated ESKD risk. Because there were few cases of ESKD in partici-



**Table 1.** Baseline characteristics of study subjects

Variable	DM status and duration				P value
	Normal	IFG	DM <5 years	DM ≥5 years	
Number	3,242,924 (67.6)	1,071,403 (22.3)	277,583 (5.8)	203,518 (4.2)	
Age, yr	45.72±13.58	50.72±12.87	55.82±12.03	62.46±10.20	<0.0001
<40	1,110,036 (34.2)	206,621 (19.3)	23,329 (8.4)	2,567 (1.3)	
40–64	1,817,602 (56.1)	706,088 (65.9)	188,288 (67.8)	114,074 (56.0)	
≥65	315,286 (9.7)	158,694 (14.8)	65,966 (23.8)	86,877 (42.7)	
Male sex	1,636,912 (50.48)	670,820 (62.61)	177,085 (63.8)	117,269 (57.62)	<0.0001
Income, low 25%	712,147 (21.96)	229,154 (21.39)	65,930 (23.75)	50,242 (24.69)	<0.0001
Smoke					<0.0001
Non	2,030,571 (62.62)	575,236 (53.69)	142,799 (51.44)	120,798 (59.35)	
Ex-smoker	443,606 (13.68)	207,272 (19.35)	57,003 (20.54)	42,523 (20.89)	
Current	768,747 (23.71)	288,895 (26.96)	77,781 (28.02)	40,197 (19.75)	
Drink					<0.0001
Non	1,678,388 (51.76)	493,466 (46.06)	144,606 (52.09)	132,518 (65.11)	
Mild	1,365,621 (42.11)	471,030 (43.96)	104,064 (37.49)	56,868 (27.94)	
Heavy	198,915 (6.13)	106,907 (9.98)	28,913 (10.42)	14,132 (6.94)	
Regular exercise	609,600 (18.80)	216,801 (20.24)	57,449 (20.70)	48,375 (23.77)	<0.0001
HTN	642,765 (19.82)	372,670 (34.78)	158,798 (57.21)	146,615 (72.04)	<0.0001
Dyslipidemia	506,435 (15.62)	265,601 (24.79)	124,162 (44.73)	109,675 (53.89)	<0.0001
BMI, kg/m <sup>2</sup>	23.33±3.18	24.48±3.25	25.30±3.46	24.76±3.21	<0.0001
Waist circumference	78.74±9.08	82.58±8.76	85.52±8.77	85.30±8.47	<0.0001
Systolic BP, mm Hg	119.79±14.19	125.47±14.65	128.39±15.29	128.54±15.51	<0.0001
Diastolic BP, mm Hg	74.95±9.74	78.34±9.94	79.49±10.17	77.35±9.89	<0.0001
Pulse pressure, mm Hg	44.8±4.5	47.0±4.7	49.4±5.1	51.5±5.6	<0.0001
Laboratory findings					
Glucose	88.14±7.36	107.46±6.43	138.59±43.20	143.06±50.58	<0.0001
eGFR, mL/min/1.73 m <sup>2</sup>	93.45±36.65	89.64±32.97	89.23±35.84	84.11±34.93	<0.0001
≥90	1,622,816 (43.4)	455,793 (42.5)	116,614 (42.0)	69,700 (34.2)	
60–90	1,535,256 (41.0)	571,573 (53.3)	142,730 (51.4)	104,550 (51.4)	
45–60	75,749 (2.0)	39,326 (3.7)	15,588 (5.6)	22,052 (10.8)	
30–45	6,706 (0.2)	3,758 (0.4)	2,149 (0.8)	5,676 (2.8)	
<30	2,397 (0.1)	953 (0.1)	502 (0.2)	1,540 (0.8)	
Proteinuria	50,499 (1.56)	23,011 (2.15)	13,007 (4.69)	16,648 (8.18)	<0.0001
Total cholesterol, mg/dL	192.85±35.20	201.89±37.26	197.02±42.06	180.97±39.33	<0.0001
HDL-C, mg/dL	56.42±17.55	54.67±17.52	51.62±16.12	50.06±15.02	<0.0001
LDL-C, mg/dL	113.2±32.6	118.72±35.43	112.37±38.76	101.25±35.81	<0.0001
Triglyceride	100.66 (100.59–100.72)	125.44 (125.31–125.57)	145.76 (145.45–146.07)	130.85 (130.55–131.16)	<0.0001

Values are presented as number (%), mean ± standard deviation, or geometric mean (95% confidence interval).

DM, diabetes mellitus; IFG, impaired fasting glucose; HTN, hypertension; BMI, body mass index; BP, blood pressure; eGFR, estimated glomerular filtration rate; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol.

**Table 2.** Adjusted risk<sup>a</sup> of ESKD according to baseline renal function and diabetic status

DM status	eGFR, mL/min/1.73 m <sup>2</sup>				
	≥90	60–90	45–60	30–45	<30
None	1 (reference)	2.2 (1.9–2.4)	20.1 (18.0–22.1)	153.1 (136.4–171.8)	501.3 (446.5–562.8)
IFG	1.2 (0.99–1.4)	2.4 (2.1–2.7)	15.1 (13.1–17.3)	108.8 (94.4–125.4)	478.5 (414.1–552.8)
<5 years	4.3 (3.8–5.0)	5.6 (4.9–6.4)	24.6 (21.3–28.5)	131.0 (112.2–152.9)	377.8 (316.5–451.3)
≥5 years	13.9 (12.4–15.7)	19.5 (18.4–22.7)	63.1 (56.4–70.5)	226.5 (202.5–253.4)	800.0 (708.1–900.3)

Values are presented as median (range).

ESKD, end-stage kidney disease; DM, diabetes mellitus; eGFR, estimated glomerular filtration rate; IFG, impaired fasting glucose.

<sup>a</sup>Hazard ratio adjusted with age, sex, income, smoke, drink, exercise, hypertension, dyslipidemia, body mass index, and proteinuria.

**Table 3.** Incidence rate (pmp) of ESKD according to baseline renal function and diabetic status

DM status	eGFR, mL/min/1.73 m <sup>2</sup>				
	≥90	60–90	45–60	30–45	<30
None	34	84	1,169	17,269	51,300
IFG	52	114	1,049	12,237	51,596
<5 years	293	404	2,327	17,127	60,667
≥5 years	1,173	1,892	7,367	35,002	142,238

pmp, per million population; ESKD, end-stage kidney disease; DM, diabetes mellitus; eGFR, estimated glomerular filtration rate; IFG, impaired fasting glucose.

pants younger than 40 years old, we divided them into two age groups at 65 years. In both groups, a strong correlation was found between diabetes duration and ESKD incidence across all eGFR categories. Notably in the younger group, both the IRs and HRs of ESKD were significantly higher than those observed in the older group, emphasizing the importance of diabetes risk stratification and targeted management in younger individuals (Table 4).

Importantly, the IFG-associated trend of increasing ESKD risk was observed only in younger participants with early-stage CKD. IFG was associated with a 1.22-fold increased risk of ESKD in stage 1 CKD and a 1.15-fold increase in stage 2 CKD. Conversely, in the older age group, no difference in ESKD risk was observed between nondiabetic and IFG groups across any eGFR category.

## DISCUSSION

This large-scale analysis of the Korean general population yielded three major findings. First, the IR of ESKD by diabetes status was 139, 188, 632, and 3,403 pmp for nondiabetes, IFG, DM duration <5 years, and ≥5 years, respectively, which is much higher than in other countries. Second, when eGFR be-

came lower than 45 mL/min/1.73 m<sup>2</sup>, the risk of ESKD increased more than 100-fold compared with those with eGFR higher than 90 mL/min/1.73 m<sup>2</sup>, even in patients without diabetes. When it comes to patients with longer duration of diabetes, the risk is more than 200-fold. This finding emphasizes the importance of preventing eGFR decline in the patients with diabetes. Third, and very importantly, in early CKD patients with eGFR ≥60 mL/min/1.73 m<sup>2</sup>, the presence of IFG was a significant risk factor for the development of new ESKD, and this finding was more pronounced in younger patients. Considering the rapidly increasing rate of ESKD in Korea, our data may not only make the general public aware of the seriousness of diabetic ESKD, but also suggest the importance of early diabetes screening and optimal glucose management even from the prediabetic status, especially in the young and early CKD patients.

According to recently published data, the global percentage of new cases of ESKD due to diabetes increased steadily in most countries from 22.1% in 2000 to 31.3% in 2015 [8]. Although the increasing trend was observed globally, there are significant differences among geographic regions. South Korea is one of the countries with the fastest increasing rates of new cases of ESKD, where about half of new cases of ESKD are

**Table 4.** Age-associated risk of ESKD by baseline renal function and diabetic status

	eGFR	DM status	Number	ESKD	Duration, person-yr	IR, pmp	HR (95% CI)	<i>P</i> <sub>interaction</sub>
Age <65 years	≥90	Normal	1,548,508	418	14,435,963.5	29	1 (ref)	<0.001
		IFG	423,054	168	3,917,647.6	43	1.22 (1.02–1.46)	
		DM <5 years	103,029	267	944,082.8	283	5.50 (4.70–6.43)	
		DM ≥5 years	54,187	621	491,581.3	1,263	19.97 (17.46–22.67)	
	60–90	Normal	1,330,787	696	12,405,358.5	56	1.81 (1.65–2.10)	
		IFG	467,465	316	4,334,460.4	73	2.00 (1.72–2.31)	
		DM <5 years	101,081	341	929,956.9	367	6.81 (5.88–7.89)	
		DM ≥5 years	53,431	1,059	483,085.0	2,192	30.92 (27.38–34.91)	
	45–60	Normal	43,894	434	405,421.4	1,070	26.12 (22.76–29.97)	
		IFG	20,306	185	186,600.3	1,000	20.99 (16.74–23.86)	
		DM <5 years	6,570	142	59,257.2	2,391	31.66 (26.04–38.50)	
		DM ≥5 years	6,737	613	57,962.1	10,571	102.89 (89.93–117.71)	
	30–45	Normal	2,813	565	23,412.9	24,123	246.01 (215.39–280.96)	
		IFG	1,320	184	11,194.4	16,431	177.38 (148.35–212.10)	
		DM <5 years	697	154	5,437.2	28,325	228.82 (189.02–277.01)	
		DM ≥5 years	1,709	632	11,662.9	54,190	367.01 (320.62–420.11)	
Age ≥65 years	≥90	Normal	74,308	100	651,807.4	153	1 (ref)	<0.001
		IFG	32,739	49	285,464.2	172	0.99 (0.77–1.39)	
		DM <5 years	13,585	43	115,690.5	372	1.77 (1.24–2.53)	
		DM ≥5 years	15,513	109	130,787.3	833	3.63 (2.77–4.77)	
	60–90	Normal	204,469	491	1,794,917.4	274	1.71 (1.38–2.12)	
		IFG	104,108	284	907,184.1	313	1.72 (1.37–2.16)	
		DM <5 years	41,649	178	354,617.9	502	2.28 (1.78–2.92)	
		DM ≥5 years	51,119	663	427,231.9	1,552	6.16 (4.99–7.61)	
	45–60	Normal	31,855	355	269,554.3	1,317	7.04 (5.64–8.79)	
		IFG	19,020	179	159,918.1	1,119	5.28 (4.13–6.75)	
		DM <5 years	9,018	168	73,958.6	2,272	9.07 (7.08–11.63)	
		DM ≥5 years	15,315	704	120,797.0	5,828	19.72 (15.90–24.33)	
	30–45	Normal	3,893	325	28,123.2	11,556	42.06 (33.59–52.67)	
		IFG	2,438	169	17,652.8	9,574	32.75 (25.55–41.97)	
		DM <5 years	1,452	111	10,035.6	11,061	35.95 (27.42–47.15)	
		DM ≥5 years	3,967	689	26,176.3	26,322	71.91 (58.22–88.80)	

ESKD, end-stage kidney disease; eGFR, estimated glomerular filtration rate; DM, diabetes mellitus; IR, incidence rate; pmp, per million population; HR, hazard ratio; CI, confidence interval; IFG, impaired fasting glucose.

caused by diabetes [7].

In South Korea, the number of people with diabetes has exceeded 6 million. With about 15.83 million people in the pre-diabetic stage, more than 20 million Koreans either have diabetes or are at risk of developing diabetes-related complica-

tions, including ESKD. In addition, the prevalence of diabetes is increasing rapidly, rising from 11.8% in 2012 to 13.8% in 2018, and 16.7% in 2020. Alarmingly, this rate continues to rise among younger individuals. Our data show that in patients younger than 65 years, the HR for diabetes-associated new



ESKD was significantly higher than in those aged 65 years or older. Furthermore, in young patients, the presence of IFG was a significant risk factor for ESKD across all eGFR groups. This is of particular concern given that 30% of people in their 30s in Korea have prediabetes.

In the case of prediabetes, about 5%–10% progress to diabetes each year, and about 40% develop diabetes in 5 years, so they can be said to be a very dangerous risk group for diabetic ESKD [17]. However, prediabetes is often overlooked as a sub-clinical period for diabetes, and the association between IFG and worsening renal function is still controversial. Indeed, in a secondary analysis of Systolic Blood Pressure Intervention Trial (SPRINT) data, IFG at baseline was not associated with the development of worsening renal function or albuminuria in participants of SPRINT [18]. However, in that study, the mean follow-up was only 3.3 years. In our data, the mean follow-up duration is about 10 years, and IFG was associated with an increased tendency of ESKD risk especially in younger patients with  $\text{eGFR} \geq 60 \text{ mL/min/1.73 m}^2$ . Supporting our data, in a 4.3-year follow-up of a Chinese community-based cohort [19], IFG was independently associated with incident albuminuria. Accordingly, we can assume that IFG is more likely to increase the risk of ESKD through progression to diabetes rather than directly increasing the incidence of ESKD. If IFG improves to nondiabetes, it may not increase the risk of ESKD. Therefore, prediabetes might be a critical stage where timely intervention can prevent the progression to full-blown diabetes and its associated complications, including ESKD.

There are several limitations to this study. First, this study may not provide new findings compared with previous research, as it is well known that the duration of diabetes and baseline renal function are associated with the risk of ESKD. However, the value of this study lies in its large size and the clarity of its presentation, which makes the complex relationships easy to understand at a glance. This approach contributes significantly to raising public awareness of kidney disease in diabetes and CKD in Korea. Second, the study is based only on the variables available in the claims data; thus, clinical information such as lifestyle, family history, and genetic factors are not accessible from the database. Third, this study only analyzed claims data of patients who underwent a health examination in 2012, so it is difficult to track the important factors that influence the development of ESKD over a longer period of time (such as changes in BMI, diabetes control, or other comorbidities). As a result, there are certain temporal limitations

in the interpretation of the data. Fourth, the diagnosis of IFG was based solely on a single fasting glucose measurement. Given that fasting blood glucose levels can exhibit significant variability, reliance on a single measurement may introduce bias into the results of the study. Fifth, there is a competing risk between death and kidney failure in DKD patients because many die before reaching ESKD [20,21]. Our analysis included only those who received renal replacement therapy and did not consider those who died before reaching ESKD. However, in Korea, many patients with diabetes receive appropriate medical care and treatment in the predialysis period and start dialysis in a timely manner. Therefore, the incidence of cardiovascular or renal death before dialysis initiation is unlikely to be much higher than in other countries.

In conclusion, understanding the high incidence of ESKD in relation to IFG as well as diabetes duration is critical to raising public awareness and warning of the seriousness of this disease. Although the risk of kidney disease related to diabetes is already well known, our results showed the surprisingly high risk of ESKD in numbers that are easy to see at a glance. In addition, our data may provide evidence to support the need for early screening for IFG or diabetes optimal intervention, and prevention strategies for eGFR decline in the general population.

## CONFLICTS OF INTEREST

Eun Roh has been associate editor of the *Diabetes & Metabolism Journal* since 2022. She was not involved in the review process of this article. Otherwise, there was no conflict of interest.

## AUTHOR CONTRIBUTIONS

Conception or design: J.K.K., K.D.H., J.G.K.  
Acquisition, analysis, or interpretation of data: H.N.J., B.J.K., B.H., J.H.H.  
Drafting the work or revising: J.K.K., E.R., J.H.K.  
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