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Trends in the prevalence of chronic kidney disease in Korean adults: the Korean National Health and Nutrition Examination Survey from 1998 to 2009

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ABSTRACT

Background. Chronic kidney disease (CKD) is associated with a poor quality of life and cardiovascular events and is a great threat to public health.

Methods. We investigated the trends of CKD prevalence over 12 years in Korean adults at least 20 years old using sampling weight methods based on the Korean National Health and Nutrition Examination Survey (KNHANES) I (1998), II (2001), III (2005) and IV (2007–09). Of the 135 954 subjects participating in KNHANES I–IV, 33 276 (14 307 men, 18 969 women) were included in the present study.

Results. The percentage of glomerular filtration rate (GFR) <60 mL/min/1.73 m^2 in KNHANES I–IV was 1.0, 5.4, 3.1 and 2.6% in men and 3.4, 9.7, 10.2 and 4.6% in women, respectively. The percentage of proteinuria ≥1+ measured by a dipstick method across KNHANES phases gradually declined in men (3.1, 3.0, 2.8 and 2.2% in KNHANES I–IV, respectively), while those in women rebounded in KNHANES IV after reduction through KNHANES III (3.3, 2.3, 1.4 and 1.9%, respectively). The prevalence of CKD (GFR <60 mL/min/1.73 m^2 or proteinuria ≥1+) in KNHANES I–IV was 3.9, 7.9, 5.4 and 4.5% in men and 6.4, 11.3, 12.0 and 6.3% in women, respectively. After stratification by age (20–39 years, 40–59 years and ≥60 years), the prevalence trends were similar to those before the stratification by sexes.

Conclusions. The prevalence of CKD in Korean adults has decreased since 2001 in men and since 2005 in women.

INTRODUCTION

In developed countries, chronic diseases such as cardiovascular disease (CVD) and cancer are the leading causes of death. Chronic kidney disease (CKD), a debilitating chronic disease, shares many of the common risk factors with CVD and is epidemiologically linked to adverse CVD morbidity and mortality [1, 2]. Patients suffering from CKD are likely to die from CVD and to progress to end-stage renal disease (ESRD) [3]. In addition, patients with CKD, especially dialysis patients, are significantly more susceptible to cognitive function impairment and infectious diseases [4, 5]. Since patients with CKD have a short life expectancy regardless of the presence of ESRD for these reasons, its socioeconomic burden on public health has a great impact. Therefore, the early identification and proper treatment of CKD can not only prevent the progression to ESRD, but can also delay death from CVD and infectious diseases.

In recent decades, there has been a worldwide increase in CKD [6, 7]. According to previous studies, ~10–15% of the adult population suffers from CKD, with a prevalence of 12.9% in Japanese, 13.0% in Chinese and 13.1% in North Americans [7–9]. The prevalence of CKD in Korean adults is lower than those of Western populations as well as those of

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other East Asian populations [10]. Furthermore, there was a decrease in the prevalence of CKD from 2005 to 2007 (8.8% in 2005 and 7.2% in 2007) according to the Korean National Health and Nutrition Examination Survey (KNHANES) [10]. However, there is a lack of studies that show how the trends of CKD prevalence in Korean adults have varied in the recent decade.

In this study, we compared the prevalence and pattern of CKD and the glomerular filtration rate (GFR) among Korean adults ≥20 years of age using data from the KNHANES for 1998, 2001, 2005 and 2007–2009, using the nationally representative samples after adjustments for sampling weights. In addition, we investigated the associations between CKD and the conventional risk factors across the KNHANES phases.

MATERIALS AND METHODS

Study population

The Korean Ministry of Health and Welfare conducted a cross-sectional and nationally representative survey on the health and nutritional status of non-institutionalized Korean civilians in KNHANES phase I (1998), II (2001), III (2005), IV (2007–09) and V (2010–12) studies. KNHANES is composed of a Health Interview Survey, a Health Behaviour Survey, a Health Examination Survey and a Nutrition Survey. Sampling units were households from which the data were collected through a stratified, multistage, probability-sampling design that was based on the sex, age and geographical area using household registries. When each KNHANES was conducted, the participants were informed that they had been randomly selected as a household to voluntarily participate in a survey. A written informed consent to use their data for further analyses was provided by all the participants who were given the right to refuse to participate in accordance with the National Health Enhancement Act. This study was based on the data obtained from KNHANES I–IV because complete data from KNHANES V had not yet been released when these analyses were conducted.

Of the 135 954 subjects participating in KNHANES I–IV, we excluded subjects younger than 20 years ($n = 40\,821$), those who did not have complete laboratory data ($n = 60\,817$) and those who did not fast overnight before examination ($n = 1040$). We also excluded those subjects who had participated in KNHANES V because the data of sampling weights for KNHANES V were not available. After these exclusions, a total of 33 276 subjects (14 307 men, 18 969 women) were included in the final analysis. This study was approved by the Institutional Review Board of Gangnam Severance Hospital, Yonsei University College of Medicine, Seoul, Korea.

Measurement of anthropometry and laboratory data

Trained medical staff performed the physical examinations following standardized procedures. Body weight and height were measured to the nearest 0.1 kg and 0.1 cm, respectively, with subjects wearing light indoor clothing without shoes. Waist circumference was measured at the narrowest point between the lower border of the rib cage and the iliac crest during exhalation. The body mass index (BMI, kg/m^2) was calculated as the ratio of weight in kilogram to squared height in meter. Blood pressure was measured twice on the right arm at 5-min intervals using a standard mercury sphygmomanometer (Baumanometer; Baum, Copiague, NY) and recorded as an average value. After an overnight fasting, blood samples were obtained from the subjects' antecubital veins. The levels of fasting plasma glucose, total cholesterol, triglycerides, high-density lipoprotein cholesterol (HDL-C) and creatinine were measured enzymatically using a 747-chemistry analyzer (Hitachi, Tokyo, Japan) in KNHANES I and II and ADVIA 1650/2400 (Siemens, NY) in KNHANES III and IV. Non-HDL-C levels were calculated using the following equation: non-HDL-C = total cholesterol – HDL-C.

Chronic kidney disease

An estimated GFR was calculated using the abbreviated equation from the Modification of Diet in Renal Disease (MDRD) study: estimated GFR (mL/min/1.73 m^2) = $186.3 \times (\text{serum creatinine}^{-1.154}) \times (\text{age}^{-0.203}) \times 0.742$ (if female) [11]. CKD was defined based on the combination of renal tissue damage or reduced renal function [12, 13]. CKD was defined as the estimated GFR <60 mL/min/1.73 m^2 or proteinuria ≥1+. Proteinuria was tested by the dipstick method using freshly voided urine samples.

Hypertension, diabetes and obesity

We stratified blood pressure into three categories: (i) normotensive, systolic blood pressure (SBP) <120 mmHg and diastolic blood pressure (DBP) <80 mmHg and no anti-hypertensive medication; (ii) prehypertensive, SBP 120–139 mmHg, 80–89 mmHg and no anti-hypertensive medication; (iii) hypertensive, SBP ≥140 mmHg, DBP ≥90 mmHg or use of anti-hypertensive medication. The glycemic status was divided into the following three categories: (i) normoglycemic, fasting plasma glucose <100 mg/dL and no anti-diabetic medication; (ii) impaired fasting glucose (IFG), fasting plasma glucose 100–125 mg/dL and no anti-diabetic medication; (iii) diabetic, fasting plasma glucose ≥126 mg/dL or use of anti-diabetic medication. The cut-off point of general obesity according to the Asia Pacific regional guideline of World Health Organization and International Obesity Task Force was defined as BMI ≥25 kg/m^2 [14].

Health-related lifestyles

Information regarding the health-related lifestyle factors was obtained from data on the self-reported questionnaire during the interview portion of each survey period. Individuals engaged in vigorous-intensity physical activity at least three times per week were categorized into the regular exercise group. Individuals drinking alcoholic beverages at least once per week were categorized into the regular drinking group. Individuals who smoked cigarettes during the relevant survey period were categorized into the current smoking group.

Statistical analysis

Data from the Korea National Statistical Office were used to define the standard population. In order to represent the entire Korean adults without biased estimates, sampling weights were used to account for the complex sampling. The demographic and biochemical characteristics of the study population were summarized using the general linear model for continuous variables and the chi-square tests for categorical variables across the KNHANES phases. All data on continuous variables were presented as means ± standard errors (SEs). The odds ratios (ORs) and 95% confidence interval (95% CI) for CKD prevalence were calculated by sex using multivariate logistic regression analyses across the KNHANES phases. In addition, we investigated the associations between the CKD prevalence risk and various clinical factors including age, lipid profile, blood pressure, glycemic status, obesity, exercise, alcoholic drinking and smoking status according to sex. All analyses were conducted using SAS statistical software (version 9.1; SAS Institute Inc., Cary, NC). All statistical tests were two-sided and the statistical significance was determined as *P*-value <0.05.

RESULTS

The percentage of men was 43.0% of the total 33 276 participants selected in the final analysis. The study population was composed of 6921 subjects in KNHANES I, 5066 subjects in KNHANES II, 5314 subjects in KNHANES III and 15 975 subjects in KNHANES IV. Table 1 shows the mean anthropometric and biochemical parameters across KNHANES phases. BMI and general obesity in men increased across the KNHANES phases, whereas those in women were the highest in KNHANES II. Across KNHANES phases, the mean SBP decreased from 127.0 to 119.1 mmHg in men and from 122.9 to 113.6 mmHg in women, although the percentages of participants taking anti-hypertensive drugs significantly increased (5.3–11.7% in men, and 7.5–14.6% in women). Total

Table 1. Subject characteristics across KNHANES phases

	I	II	III	IV	*P*-value
Men					
N	3079	2187	2251	6790	
Age (years)	42.6 ± 0.4	46.0 ± 0.5	42.6 ± 0.4	43.7 ± 0.3	<0.001
BMI (kg/m^2)	23.2 ± 0.1	23.6 ± 0.1	24.0 ± 0.1	24.1 ± 0.1	<0.001
General obesity (%)[a]	25.7 ± 1.0	31.5 ± 1.2	35.1 ± 1.2	36.4 ± 0.7	0.009
SBP (mmHg)	127.0 ± 0.4	126.8 ± 0.6	121.1 ± 0.4	119.1 ± 0.3	<0.001
DBP (mmHg)	81.0 ± 0.3	80.4 ± 0.3	80.2 ± 0.4	79.6 ± 0.2	<0.001
Anti-hypertensives (%)[a]	5.3 ± 0.4	8.3 ± 0.7	9.3 ± 0.7	11.7 ± 0.5	<0.001
Hypertension (%)[a]	28.4 ± 1.0	30.7 ± 1.3	25.3 ± 1.1	27.1 ± 0.8	<0.001
Fasting plasma glucose (mg/dL)	101.5 ± 0.7	98.6 ± 0.5	95.6 ± 0.5	97.3 ± 0.4	<0.001
Anti-diabetics (%)[a]	3.6 ± 0.3	4.2 ± 0.5	3.5 ± 0.4	5.1 ± 0.3	0.003
Diabetes (%)[a]	10.9 ± 0.7	7.9 ± 0.7	7.0 ± 0.6	8.5 ± 0.4	<0.001
Total cholesterol (mg/dL)	186.9 ± 1.0	189.8 ± 0.9	183.6 ± 0.9	185.7 ± 0.6	<0.001
Triglycerides (mg/dL)	133.5 ± 1.6	159.4 ± 2.4	156.5 ± 3.7	153.8 ± 1.7	<0.001
HDL-C (mg/dL)	47.8 ± 0.3	43.6 ± 0.3	42.5 ± 0.3	45.9 ± 0.3	<0.001
Non-HDL-C (mg/dL)	139.1 ± 1.0	146.2 ± 0.9	141.1 ± 0.8	139.8 ± 0.7	<0.001
Anti-dyslipidemics (%)[a]	NA	NA	1.0 ± 0.2	2.0 ± 0.2	0.002
Regular exercise (%)[a]	10.7 ± 0.7	14.9 ± 1.0	20.3 ± 1.1	19.5 ± 0.7	0.003
Regular drinker (%)[a]	74.0 ± 0.9	48.4 ± 1.3	53.4 ± 1.5	36.6 ± 0.8	<0.001
Current smoker (%)[a]	65.6 ± 1.1	59.8 ± 1.3	48.0 ± 1.4	46.5 ± 0.8	<0.001
Creatinine (mg/dL)	1.00 ± 0.00	1.10 ± 0.00	1.07 ± 0.01	1.03 ± 0.00	<0.001
GFR (mL/min/1.73 m^2)	90.5 ± 0.5	79.3 ± 0.4	82.8 ± 0.4	87.3 ± 0.4	<0.001
Proteinuria (%)[a]	3.1 ± 0.4	3.0 ± 0.4	2.8 ± 0.4	2.2 ± 0.3	0.223

Continued

Table 1. Continued

	I	II	III	IV	*P*-value
Women					
N	3842	2879	3063	9185	
Age (years)	43.7 ± 0.4	45.7 ± 0.4	44.3 ± 0.4	45.6 ± 0.3	<0.001
BMI (kg/m^2)	23.2 ± 0.1	23.5 ± 0.1	23.3 ± 0.1	23.2 ± 0.1	<0.001
General obesity (%)[a]	27.4 ± 0.8	29.6 ± 1.1	28.0 ± 1.1	27.6 ± 0.6	0.325
SBP (mmHg)	122.9 ± 0.5	120.4 ± 0.6	114.8 ± 0.5	113.6 ± 0.3	<0.001
DBP (mmHg)	75.9 ± 0.3	75.2 ± 0.3	74.1 ± 0.3	73.6 ± 0.2	<0.001
Anti-hypertensives (%)[a]	7.5 ± 0.5	9.9 ± 0.7	12.2 ± 0.7	14.6 ± 0.5	<0.001
Hypertension (%)[a]	22.1 ± 0.9	22.9 ± 1.1	20.0 ± 0.9	21.9 ± 0.6	<0.001
Fasting plasma glucose (mg/dL)	100.1 ± 0.7	96.8 ± 0.5	92.3 ± 0.5	94.6 ± 0.3	<0.001
Anti-diabetics (%)[a]	3.6 ± 0.3	3.8 ± 0.4	3.5 ± 0.4	4.6 ± 0.3	0.043
Diabetes (%)[a]	8.3 ± 0.6	6.8 ± 0.5	5.9 ± 0.5	6.8 ± 0.3	<0.001
Total cholesterol (mg/dL)	187.7 ± 0.7	188.6 ± 0.8	182.9 ± 0.8	187.0 ± 0.6	<0.001
Triglycerides (mg/dL)	108.5 ± 1.2	124.3 ± 1.6	111.4 ± 1.6	113.2 ± 1.2	<0.001
HDL-C (mg/dL)	51.9 ± 0.3	47.9 ± 0.3	47.5 ± 0.2	51.4 ± 0.3	<0.001
Non-HDL-C (mg/dL)	135.8 ± 0.7	140.5 ± 0.8	135.4 ± 0.8	135.6 ± 0.7	<0.001
Anti-dyslipidemics (%)[a]	NA	NA	1.2 ± 0.2	2.9 ± 0.2	<0.001
Regular exercise (%)[a]	8.5 ± 0.6	11.6 ± 0.8	12.4 ± 0.9	14.1 ± 0.5	0.045
Regular drinker (%)[a]	31.7 ± 1.2	10.0 ± 0.7	16.2 ± 0.9	9.6 ± 0.4	<0.001
Current smoker (%)[a]	6.3 ± 0.5	4.7 ± 0.5	5.0 ± 0.5	6.3 ± 0.3	0.010
Creatinine (mg/dL)	0.82 ± 0.00	0.87 ± 0.00	0.92 ± 0.00	0.79 ± 0.00	<0.001
GFR (mL/min/1.73 m^2)	83.7 ± 0.4	77.8 ± 0.4	73.4 ± 0.5	88.3 ± 0.6	<0.001
Proteinuria (%)[a]	3.3 ± 0.3	2.3 ± 0.3	1.4 ± 0.3	1.9 ± 0.2	0.123

All data except general obesity, anti-hypertensives, hypertension, anti-diabetics, diabetes, anti-dyslipidemics, regular exercise, regular drinker, current smoker and proteinuria are represented as mean (SE) and the *P*-values are determined by the general linear models.
BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; HDL-C, high-density lipoprotein cholesterol; GFR, glomerular filtration rate.
[a]General obesity, anti-hypertensives, hypertension, anti-diabetics, diabetes, anti-dyslipidemics, regular exercise, regular drinker, current smoker and proteinuria are represented as percentage and the *P*-values are determined by chi-square tests.

cholesterol and triglyceride levels in both sexes were highest in KNHANES II, while the HDL-C levels were lowest in KNHANES III. The percentage of participants taking anti-diabetic drugs (3.6–5.1% in men, 3.6–4.6% in women) increased between KNHANES I and IV, while the percentage of participants taking anti-dyslipidemic drugs (1.0–2.0% in men, 1.2–2.9% in women) increased between KNHANES III and IV. The number of participants who were engaged in regular exercise increased across the KNHANES phases, except KNHANES IV in men. The number of participants regularly drinking alcoholic beverages was extraordinarily high in KNHANES I (74.0% in men, 31.7% in women). Men in KNHANES II had the highest level of serum creatinine (1.10 mg/dL) and the lowest level of GFR (79.3 mL/min/1.73 m^2), while women in KNHANES III had the highest level of serum creatinine (0.92 mg/dL) and the lowest level of GFR (73.4 mL/min/1.73 m^2).

The prevalence of GFR <60 mL/min/1.73 m^2, proteinuria and CKD was calculated. The percentages of GFR <60 mL/min/1.73 m^2 in KNHANES I–IV were 1.0, 5.4, 3.1 and 2.6% in men and 3.4, 9.7, 10.2 and 4.6% in women, respectively (*P* for trend <0.001 in both sexes) (Figure 1A). The percentage of proteinuria using dipstick ≥1+ in random urine samples across the KNHANES phases tended to decline in men (3.1, 3.0, 2.8 and 2.2% from KNHANES I–IV), while those in women rebound in KNHANES IV after reduction through KNHANES III (3.3, 2.3, 1.4 and 1.9%) (Figure 1B). The prevalence of CKD (GFR <60 mL/min/1.73 m^2 or proteinuria

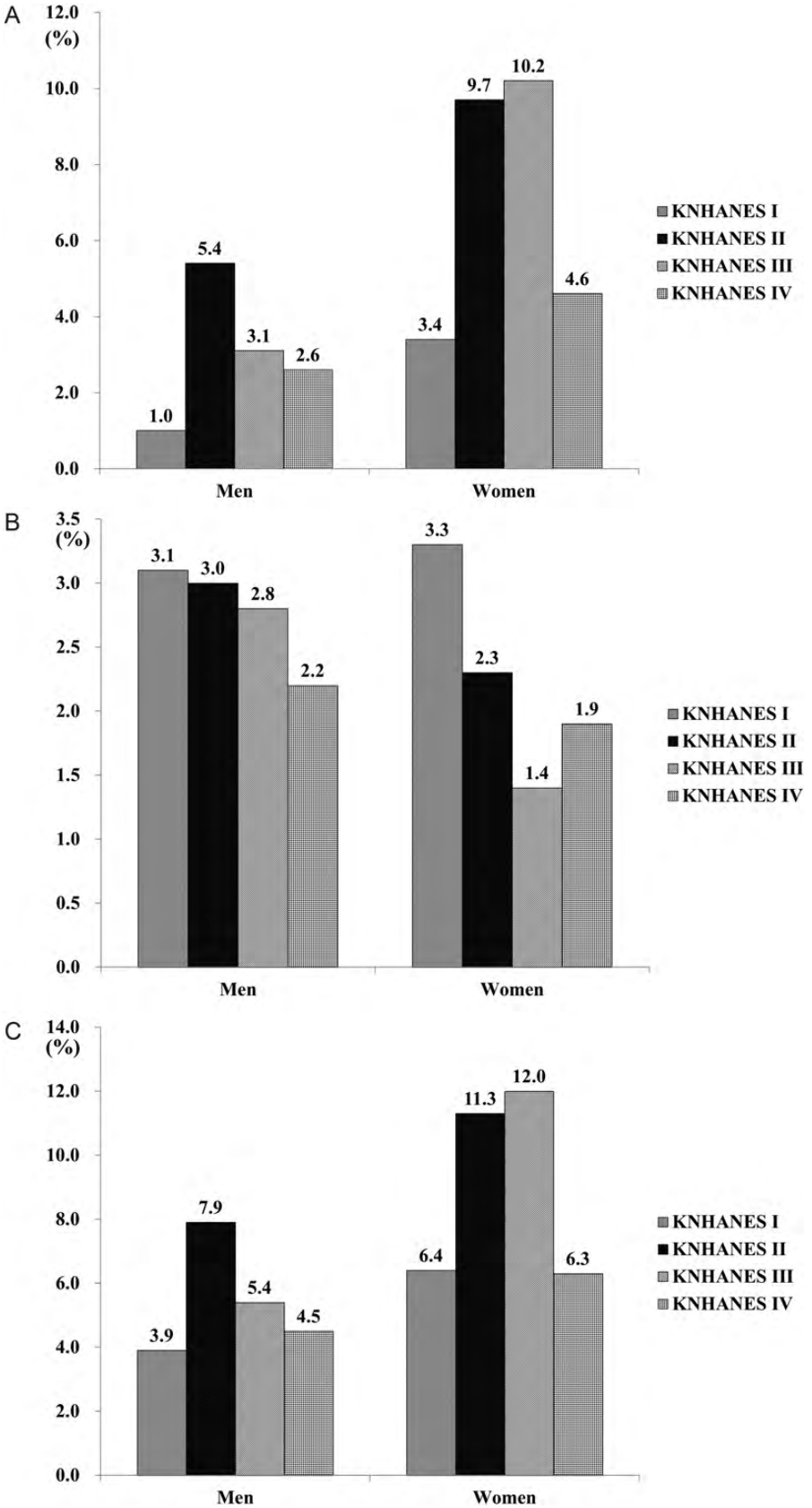

FIGURE 1: Prevalence of CKD according to the KNHANES phase. (A) Prevalence of the GFR <60 mL/min/1.73 m^2 according to the KNHANES phase ($P < 0.001$ and P for trend <0.001 in both the sexes). (B) Prevalence of proteinuria according to the KNHANES phase (men: P-value = 0.223 and P for trend 0.089, women: P-value 0.122 and P for trend 0.676). (C) Prevalence of CKD (GFR <60 mL/min/1.73 m^2 or proteinuria) according to the KNHANES phase ($P < 0.001$ and P for trend < 0.001 in both the sexes). All P-values are as determined by chi-square tests.

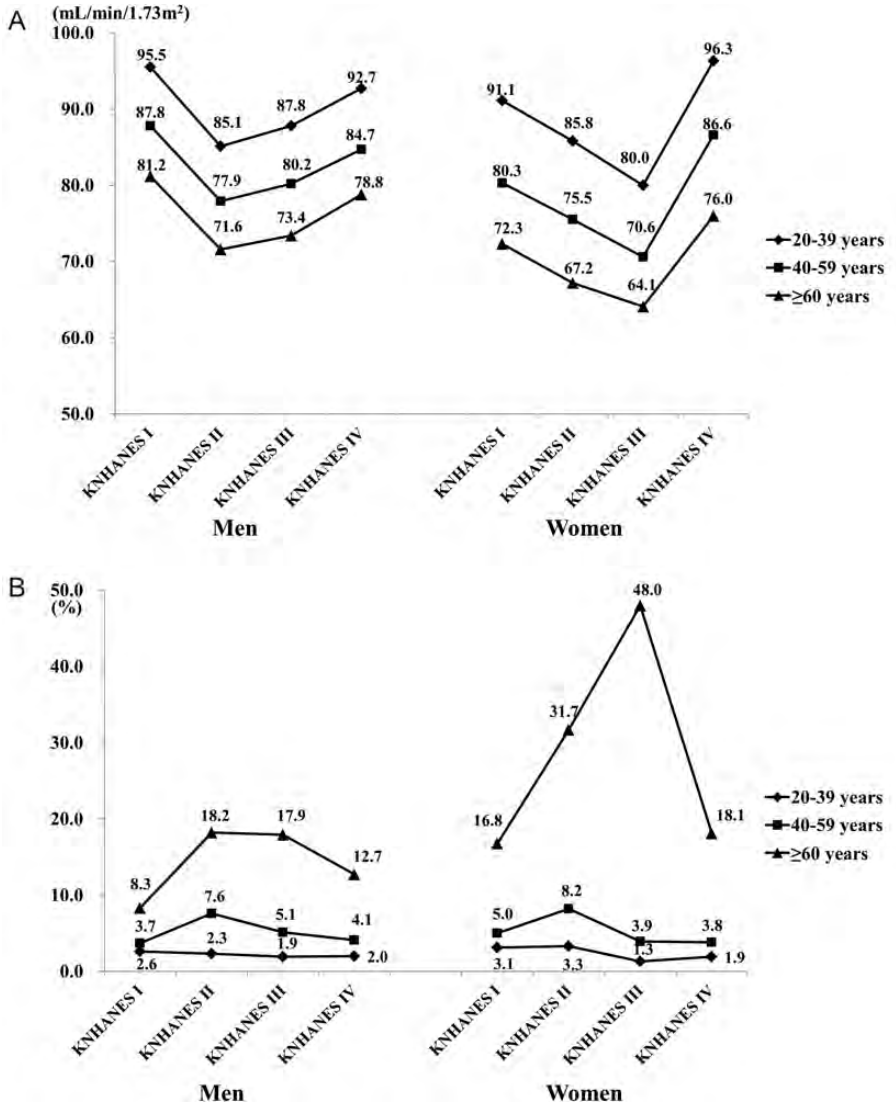

FIGURE 2: Trends of estimated GFR and prevalence of CKD according to the age group and KNHANES phase. (A) Estimated GFR according to the age group and KNHANES phase. All *P*-values as determined by the general linear models were <0.05. (*B*) Prevalence trends of CKD according to the age group and KNHANES phase. All *P*-values are as determined by chi-square tests. The *P*-values are 0.859 in 20–39 years, 0.007 in 40–59 years and 0.013 in ≥60 years in men, 0.029 in 20–39 years, <0.001 in 40–59 years and <0.001 in ≥60 years in women.

≥1+) was 3.9, 7.9, 5.4 and 4.5% in men and 6.4, 11.3, 12.0 and 6.3% in women in KNHANES I–IV, respectively (*P* for trend <0.001 in both sexes) (Figure 1C).

We compared the GFR in each survey phase according to the age group (20–39 years, 40–59 years, ≥60 years). The oldest group had the lowest mean GFR in both sexes regardless of the KHNANES phase (Figure 2A). The mean GFRs were the lowest in KNHANES II in men, while those in women were the lowest in KNHANES III regardless of the age group. Contrary to the mean GFR, the prevalence trends of CKD in each age group according to the KNHANES phase were different from those of CKD, which were calculated after including all participants. The CKD prevalence in men aged 40–59 years and at least 60 years was the highest in KNHANES II (7.6% in 40–59 years, 18.2% in at least 60 years), while that in men aged 20–39 years was not significantly changed ($P = 0.859$) (Figure 2B). The prevalence of CKD was the highest in KNHANES III in women at least 60 years of age (48.0%) and in KNHANES II in women 20–39 years old and 40–59 years old (3.3 and 8.2%, respectively).

The results of the statistical tests for trends in CKD prevalence over the 12 years of the survey cycles between 1998 and 2009 were expressed as ORs (95% CIs), which indicated the change in the OR for CKD according to the KNHANES phase (Figure 3). Compared with KNHANES I, the ORs for CKD in men increased in KNHANES II and then decreased. The ORs for CKD in women waned rapidly through KNHANES III.

In order to investigate the associations between CKD and conventional risk factors across the KNHANES phases, logistic regression analyses were conducted after adjusting for age, non-HDL-C, triglycerides, HDL-C, blood pressure, glycemic status, obesity, exercise status, drinking status, smoking status and KNHANES phase (Table 2).

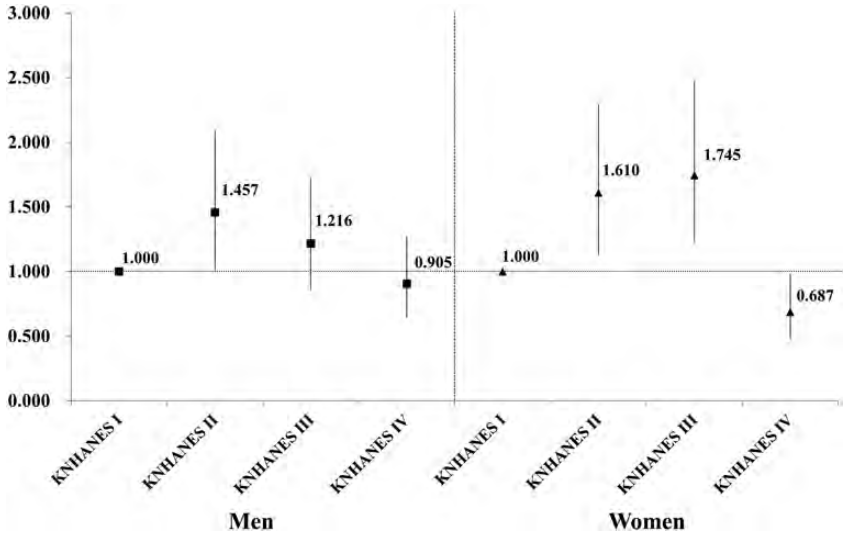

FIGURE 3: Estimated change in the ORs for CKD over 12 years. Logistic regression analyses were adjusted for age, non-HDL-C levels, triglycerides, HDL-C levels, blood pressure (normotensive, prehypertensive, hypertensive), glycemic status (normoglycemic, impaired fasting glucose, diabetes), obesity (non-obese, obese), exercise status (<3/week, ≥3/week), drinking status (<1/week, ≥1/week) and smoking status (non-current, current).

Compared with the normotensive population, hypertensive population was associated with the prevalence of CKD in both sexes [2.119 (1.547–2.902) in men, 1.318 (1.069–1.626) in women]. Compared with subjects with normoglycemic status, the ORs of subjects with diabetes were significantly higher [1.922 (1.486–2.485) in men, 1.857 (1.494–2.308) in women]. The numbers of CKD were positively associated with age and non-HDL-C levels, while it was negatively associated with HDL-C levels in both sexes. Only the male subjects who were engaged in regular exercise or who regularly drank alcoholic beverages were negatively associated with the prevalence risk of CKD.

DISCUSSION

The major finding of this study is that the prevalence of CKD appears to have decreased since 2001 in men and since 2005 in women using a nationally representative sample of Korean adults 20 years of age or older.

Although the prevalence of CKD differs according to ethnicity, most studies report that this prevalence seems to be increasing worldwide [6, 7]. Coresh *et al.* reported that the CKD prevalence increased from 10 to 13% in the US population (age ≥20 years old) between 1988 and 2004 [7]. Nagata *et al.* demonstrated that there were upward trends of CKD prevalence from 13.8 to 22.1% in Japanese men (age ≥40 years old) but not in women between 1974 and 2002, respectively [6]. Despite these global increasing trends of CKD prevalence, there is a lack of research using the up-to-date data over a long period. Contrary to previous studies, Lee *et al* reported that the CKD prevalence in the Korean population decreased between 2005 (KNHANES III) and 2007 (the first year of KNHANES IV) [10]. Our study confirmed the results of the previous study by Lee *et al.*, using data collected for a longer duration (12 years) after stratification according to the age group and sex. Furthermore, the OR for CKD across KNHANES phases began to decrease, particularly in women, even after adjusting for other covariates including age, non-HDL-C, triglycerides, HDL-C, blood pressure, glycemic status, obesity, exercise status, drinking status and smoking status. The results of logistic regression analysis demonstrated that older age, high non-HDL-C levels, low HDL-C levels, hypertension and diabetes were positively related to CKD in both sexes, while regular exercise and alcoholic consumption were negatively related to CKD only in men, but not in women (Table 2). The decreased prevalence of CKD in Korean adults in recent survey phases can be partly explained by the combined effect of not only active management of chronic diseases such as hypertension, diabetes and dyslipidemia, but also the increased number of subjects who were regularly engaged in exercise.

Hypertension is the strongest risk factor and consequence of CKD [15, 16]. Although the subjects with hypertension had a higher risk of developing CKD than those without hypertension, well-controlled blood pressure and certain classes of anti-hypertensive medications such as angiotensin-converting enzyme (ACE) inhibitors or angiotensin receptor blockers (ARBs) can delay or prevent the development of CKD and the progression to ESRD [17]. The number of subjects taking anti-hypertensive drugs increased across KNHANES I–IV, whereas the mean blood pressure levels decreased in both men and women. The percentage of individuals with well-controlled blood pressure (SBP <120 mmHg and DBP <80 mmHg) have been increasing across the KNHANES phases in both sexes (Supplementary Appendix Table 1). It seems that active management of high blood pressure, increasing rate of individuals with adequate blood pressure and proper choice of renoprotective anti-hypertensive agents such as ACE inhibitors and ARBs in a high-risk

Table 2. Logistic regression analyses for CKD by sex

All	Men OR (95% CI)	Women OR (95% CI)
Blood pressure		
Prehypertensive versus normotensive	1.160 (0.833, 1.615)	0.790 (0.640, 0.974)
Hypertensive versus normotensive	2.119 (1.547, 2.902)	1.318 (1.069, 1.626)
Glucose level		
IFG versus normoglycemic	1.253 (0.968, 1.621)	1.142 (0.941, 1.387)
Diabetes versus normoglycemic	1.922 (1.486, 2.486)	1.857 (1.494, 2.308)
Obesity (BMI <25 kg/m^2 versus ≥25 kg/m^2)	1.173 (0.937, 1.468)	1.119 (0.947, 1.322)
Age (10 years)	1.536 (1.372, 1.719)	2.002 (1.838, 2.181)
Non-HDL-C (10 mg/dL)	1.067 (1.031, 1.105)	1.038 (1.012, 1.064)
Triglycerides (10 mg/dL)	1.002 (0.994, 1.009)	0.998 (0.988, 1.008)
HDL-C (10 mg/dL)	0.835 (0.737, 0.945)	0.842 (0.770, 0.921)
Regular exercise (yes versus no)	0.712 (0.530, 0.957)	0.822 (0.615, 1.099)
Regular drinking (yes versus no)	0.680 (0.532, 0.870)	1.016 (0.752, 1.373)
Current smoking (yes versus no)	0.911 (0.734, 1.130)	1.217 (0.861, 1.721)

Adjusted for blood pressure (normotensive, prehypertensive, hypertensive), glycemic status (normoglycemic, impaired fasting glucose, diabetes), obesity (non-obese, obese), age, non-HDL-C levels, triglycerides, HDL-C levels, exercise status (<3/week, ≥3/week), drinking status (<1/week, ≥1/week), smoking status (non-current, current) and KNHANES phase.
IFG, impaired fasting glucose; BMI, body mass index; HDL-C, high-density lipoprotein cholesterol.

population reduced CKD prevalence in the Korean adults. In a previous study, Yano *et al.* demonstrated that women in prehypertension with normal blood pressure (SBP = 120–129 mmHg and/or DBP = 80–84 mmHg) were negatively associated with CKD, similarly to our findings, while men in prehypertension with high-normal blood pressure (SBP = 130–139 mmHg and/or DBP = 85–89 mmHg) were positively associated [18]. However, this study showed that prehypertension in women was negatively associated with CKD (Table 2). This discrepancy might happen because we did not elaborately stratify prehypertension into prehypertension with normal blood pressure and prehypertension with high-normal blood pressure as in Yano's study. In addition, obesity might play a role as an intermediate confounder to inversely link prehypertension and CKD. In order to control for obesity as an intermediate confounder, we conducted logistic regression analyses after stratifying the entire population into a non-obese (BMI <25 kg/m^2) and obese group (BMI ≥25kg/m^2). After this stratification, there was no statistically significant relationship in women (Supplementary Appendix Table 2). There is a possibility that the inverse association between prehypertension and CKD in women was an epiphenomenon and was mediated by obesity as an intermediate variable. Diabetes mellitus is also considered to be an important contributor to the development of CKD in addition to its integral role in hypertension [19]. Similarly to anti-hypertensive medication and blood pressure control, the percentage of subjects taking anti-diabetic drugs slightly increased between KNHANES I and IV. The mean fasting blood glucose levels were better controlled in the recent two phases (III and IV) than in the previous two phases (I and II). Some types of anti-diabetic drugs such as biguanide and thiazolidinedione have a renoprotective role in the development and progression of CKD through insulin-sensitizing, antioxidant and anti-inflammatory properties [20–22]. Thus, adequate choice of anti-diabetic medication and improved glycemic control could reduce CKD prevalence. Although the controversy exists about which type of dyslipidemia plays a more dominant role in the development and progression of CKD, it is certain that dyslipidemia is another risk factor for CKD [23–26]. Anti-dyslipidemic agents including 3-hydroxy-3-methyl-glutaryl-CoA reductase inhibitor and omega 3-fatty acids can delay progressive kidney impairment since they improve the blood lipid profile and endothelial function and have anti-inflammatory and antioxidative properties [27–29]. Unfortunately, the data regarding lipid-lowering medications were not collected in KNHANES I and II. The percentage of subjects who were engaged in regular exercise at least three times per week gradually increased across KNHANES phases. Regular exercise prevents and decreases insulin resistance and dyslipidemia through the activation of lipoprotein lipase and lecithin cholesterol acyltransferase. Regular exercise also deactivates cholesterol ester transport proteins, leading to the reduction of total cholesterol and triglycerides and the elevation of HDL-C [30–33]. Accordingly, increased physical activity could be partly associated with the reduced CKD prevalence in Korean population in the recent years. Moderate-to-high alcohol consumption contributes to the

development of albuminuria [34]. The percentage of subjects who regularly drink alcoholic beverages was far higher in KNHANES I than those in the other KNHANES phases. This finding may be linked to the Asian financial crisis in Korea since late 1997. The higher percentage of regular drinkers may be associated with a higher prevalence of proteinuria in KNHANES I. However, we did not use the total amount of alcohol consumption, so the dose-response between alcohol consumption and kidney impairment such as GFR and proteinuria could not be calculated.

Some limitations should be considered when interpreting this study. It is difficult to determine the actual factors that lead to the reduced prevalence of CKD. Although the multivariate logistic regression analyses demonstrated that hypertension, diabetes, aging, high non-HDL-C levels and low HDL-C levels in both sexes and low levels of physical activity and regular alcohol consumption in men were associated with CKD risk, what kinds of factors reduced the prevalence trends of CKD in Korea could not be determined. The Kidney Disease Outcomes Quality Initiative guideline defines CKD as the presence of either renal dysfunction (GFR <60 mL/min/1.73 m^2) or renal damage (proteinuria or albuminuria) lasting for ≥3months [13]. However, we defined CKD using a single measurement of the estimated GFR based on the MDRD equation and of proteinuria by a dipstick test. The estimated GFR calculated by the MDRD formula may not accurately estimate the actual GFR, especially in the Asian population, because it was developed using the study samples of subjects of primarily European descent. Thus, if an equation capable of estimating GFRs in Koreans were developed, we could more correctly estimate the GFR. A substantial number of participants ($n = 60\,817$) were excluded because of missing laboratory data. For these reasons, there is a possibility of selection bias despite the large representative study population with sampling weights. The urine samples collected in the KNHANES phases were not the first voided urine in the morning and were not measured quantitatively. Nevertheless, we considered that these limitations did not strongly affect our conclusion because our data came from a large number of participants over sufficient study duration.

Despite the potential limitations, this study has several strengths. First, we showed the trends of CKD over a relatively long period (12 years). Second, the data were based on a nationally representative population. Third, sampling weights were applied to all analyses to maintain the representativeness of Korean adults. Finally, we adjusted for multiple risk factors in order to demonstrate how the prevalence trends of CKD were changed regardless of other factors such as age, hypertension, diabetes, dyslipidemia and health-related behaviours. Thus, our findings are generalizable and representative in Korean adults.

In conclusion, the prevalence of CKD in Korean adults has decreased since 2001 in men and since 2005 in women. This trend change can be partially explained by the combination of the beneficial effects of proper management of cardiometabolic diseases and increased physical exercise.

SUPPLEMENTARY DATA

Supplementary data are available online at http://ndt.oxfordjournals.org.

CONFLICT OF INTEREST STATEMENT

None declared.

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