Original Paper

Is Alcohol Drinking Associated with Renal Impairment in the General Population of South Korea?

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Key Words

Heavy drinking • Binge drinking • Renal dysfunction • Glomerular filtration rate • Albuminuria

Abstract

Background/Aims: We examined relationships between the average amount of daily alcohol intake, drinking patterns, and renal dysfunction among South Korean adults aged ≥ 20 years. **Methods:** The analysis used data from the Korean National Health and Nutrition Examination Survey (KNHANES), a cross-sectional survey of Korean civilians, conducted from January to December 2011. In this study, a sample of 5,251 participants was analysed. **Results:** Compared with abstinence, the odds ratio for a decrease in estimated glomerular filtration rate (eGFR) was 0.14 (95% CI: 0.01-0.91) among heavy drinkers, and 0.42 (95% CI: 0.17-0.98) among binge drinkers and the association between the amount of mean daily alcohol intake, binge-drinking status and a likelihood of reduced eGFR value showed significant trends ($p = 0.041$ and $p = 0.038$, respectively), after adjusting for age, smoking status, amount of physical activity, morbid hypertension, diabetes, dyslipidaemia, anaemia and body mass index. There was no significant association between alcohol consumption and the urine albumin to creatinine ratio in men, or between alcohol consumption and renal dysfunction in women. **Conclusions:** Alcohol consumption was inversely associated with a reduction in eGFR in Korean men. However, these findings should be interpreted cautiously, given the other harmful effects related to alcohol consumption, especially heavy and binge drinking.

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Introduction

Renal insufficiency, the presence of kidney damage or decreased kidney function, is a significant public health problem, due to the increase in the prevalence [1-3] and the economic burden of it [4]. Furthermore, renal insufficiency has been recognised as a

predictor of cardiovascular disease [5]. The understanding of factors that associate with the risk of renal insufficiency might help to decrease the prevalence or the burden of renal insufficiency.

Alcohol drinking is common in the general population, and is a well-known risk factor for various diseases. In addition, excessive alcohol consumption has been linked to increased cardiovascular risk and mortality [6, 7] whereas moderate alcohol consumption has been associated with a decreased risk of cardiovascular disease [8, 9]. Thus, it is evidently critical to evaluate alcohol drinking as the risk factor associated with renal insufficiency. However, recent studies performed to investigate the relationship of alcohol drinking and renal insufficiency have reported inconsistent results. Some studies in the general population have reported that alcohol consumption is inversely associated with the renal dysfunction or the incidence of chronic renal disease [10-14], whereas others have reported that alcohol consumption is positively related to renal impairment [15, 16], or that there is no relationship between alcohol consumption and renal function [14, 17, 18]. Furthermore, there were no studies on alcohol consumption and renal function in Korean population, and the results of previous studies in other populations may be difficult to generalise to Korean populations due to ethnic differences [10, 15-20] or dissimilar population subgroups [11, 12, 18]. The lack of evidence about the influence of alcohol drinking on renal function has limited the use of controls on alcohol drinking as a method for preventing and monitoring the progression of renal insufficiency.

To evaluate the relationship between alcohol consumption and renal dysfunction, alcohol consumption should be considered in two dimensions: average volume of alcohol intake and the pattern of drinking [21]. The average volume of alcohol consumed as an alcohol-related variable has been used in most studies of alcohol consumption and renal function. Additionally, the pattern of drinking is an important factor to consider in alcohol-related health issues [22], especially binge drinking, high-volume drinking occasions [21, 23]. In some studies, a rise in platelet reactivity and thrombosis was reported during withdrawal after binge drinking, and this may be involved in the detrimental effects of binge drinking [21, 22, 24]. To date, however, little is known about any association between not only the average volume of alcohol consumed but also binge drinking as a pattern of drinking, and kidney dysfunction.

We investigated the relationships between the average amount of daily alcohol intake, binge drinking and renal dysfunction, using data from the South Korean population, based on a representative nationwide survey.

Materials and Methods

The Korean National Health and Nutrition Examination Survey (KNHANES) is performed by the Korea Centre for Disease Control and Prevention (KCDC) at 3-year intervals to assess the status of public health and to provide baseline data for the development, establishment, and evaluation of public health policies in the Korean population. In KNHANES, participants include non-institutionalised individuals aged ≥ 1 year by a stratified, multi-stage cluster probability sampling design to ensure an independent and homogeneous sampling each year in addition to nationally representative sampling. Data are collected by a variety of means including household interviews, physical examinations carried out with anthropometric and biochemical measurements, and the assessment of nutritional status [25]. We used data from the KNHANES V-2 performed during the period from January to December 2011. In total, 10,589 participants were recruited and 8,518 of them completed the KNHANES V-2 (participation rate: 80.4%). All the protocols were approved by the Institutional Review Board of the KCDC and the participants provided written informed consent at baseline.

Study population

In this cross-sectional study, we originally examined 8,518 participants based on data collected from KNHANES V-2. Inclusion criteria for the current study were age ≥ 20 years, so we excluded 1,952 participants

aged 20 years or younger. We also excluded participants with pregnancy (n = 27), known renal failure (n = 14), and missing information or values for the major variables (n = 1,274). The population for the current study thus consisted of 5,251 participants.

The current study was approved by the Institutional Review Board of the Catholic University of Korea (IRB approval number: VC13RISI0221).

Variables and evaluation criteria

a) Alcohol consumption. Information on alcohol consumption included the frequency of drinking days, number of drinks consumed per drinking day, and the frequency of binge drinking during the 1 year that preceded the interview for KNHANES V-2. We used the Korean version of a “standard drink” (any drink that contains 12 g of pure alcohol) based on 4.5 vol% in beer, 12 vol% in wine, 6 vol% in Korean traditional makgeolli, 20 vol% in Korean soju, and 40 vol% in whisky [26]. We converted the frequency of drinking days and the number of drinks consumed per drinking day into mean daily alcohol intake (gram pure alcohol/day). Using the WHO classification [21], we classified mean daily alcohol intake into three categories: abstinence (not having had a drink containing alcohol within the last year), moderate drinking (women, 0.1-19.99 g pure alcohol/day; men, 0.1-39.99 g pure alcohol/day), and heavy drinking (women, ≥ 20 g pure alcohol/day; men, ≥ 40 g pure alcohol/day). Binge drinking is defined as consuming ≥ 5 standard drinks (≥ 4 drinks for women) consecutively on one occasion [27], and the data were subcategorised into three groups based on binge drinking: abstinence, non-binge drinking, and binge drinking.

(b) Renal function. We evaluated the renal function using estimated glomerular filtration rate (eGFR) and the urine albumin to creatinine ratio (ACR) from data on KNHANES V-2. The GFR was estimated using the re-expressed “Modification of Diet in Renal Disease” (MDRD) study equation using calibrated serum creatinine values [28], and the formula for eGFR is:

$$175 \times (\text{serum creatinine concentration})^{-1.154} \times (\text{age})^{-0.203}$$

and multiplied by a factor of 0.742 for women, where creatinine is measure in mg/dL, age in years, and the eGFR units are mL/min/1.73 m². A reduced eGFR value, a clinical marker of renal dysfunction, was defined as ≤ 60 mL/min/1.73 m² [29]. The urine ACR was measured from an untimed spot urine sample. The albumin concentration and creatinine in urine were determined by a turbidimetric assay and a colorimetric analysis, respectively (Hitachi Automatic Analyser 7600, Hitachi, Japan). An elevated urine ACR value, as a clinical marker of renal dysfunction, was defined as ≥ 30 mg/g or greater [29].

(c) Covariates. Age, body mass index (BMI, kg/m²), diabetes, hypertension, dyslipidaemia, anaemia, smoking, and physical activity were assessed as covariables. Age and BMI were categorised as continuous variables, known diabetes, hypertension, dyslipidaemia as well as anaemia defined as a hemoglobin concentration < 13 g/dL for men and < 12 g/dL for women [30] were categorised as yes or no, smoking status was classified as smoker or non-smoker currently, and physical activity was classified as sufficient or not. Sufficient physical activity defined as 150 min or more of moderate-intensity or 75 min or more of vigorous-intensity physical activity per week [31].

Data analysis

To analyse the data through a complex sample design, we used the SAS PROC SURVEY module, considering strata, clusters, and weights. All analyses were carried out using the sample weights of KNHANES. Gender-specific characteristics of the study population were analysed using independent t tests for continuous variables and the chi-squared test for dichotomous variables. The data are expressed as means (standard error) or percentages, and the geometric mean and 95% confidence interval (CI) for skewed distributions. The distribution of eGFR and urine ACR values according to categories of alcohol consumption was analysed using the chi-squared test. The eGFR values were classified into three categories: GFR ≥ 90, 60-89, and < 60 mL/min/1.73 m², and urine ACR values classified into three categories: urine ACR < 30, 30-299, and ≥ 300 mg/g [29]. To identify renal function according to mean daily alcohol consumption and binge drinking, we performed analysis of covariance (ANCOVA), adjusted for age, smoking status, amount of physical activity, morbid state of hypertension, diabetes, dyslipidaemia, anaemia and BMI. The correlation between alcohol consumption and renal dysfunction was analysed using a multiple logistic regression after adjusting for all covariates above. All statistical analyses were performed using the SAS software (ver. 9.2; SAS Institute, Cary, NC). P-values of < 0.05 were considered to indicate statistical significance.

Results

Study population characteristics

As shown in Table 1, 45.4% (n = 2,386) of the 5,251 participants were men. In men, 12.3% (n = 293) reported abstinence compared with 33.1% (n = 948) of women. Most participants, both men and women, were moderate drinkers with regard to the mean daily alcohol intake (77.1% and 61.5%, respectively). With respect to binge drinking, the prevalence was higher in men (74.1%) than women (37.6%). There was a difference between the men and women regarding the values of age, smoking status, physical activity, BMI, prevalence of hypertension, diabetes, dyslipidaemia, anaemia, and levels of blood pressure, fasting glucose, hemoglobin, and total

cholesterol. In women, higher eGFR values and lower urine ACR values were observed than men (p < 0.001). The prevalence of renal dysfunction, defined as eGFR < 60 mL/min/1.73 m² was not statistically significantly different between men and women (1.9% and 1.7%, respectively; p = 0.588), while participants with urine ACR ≥ 30 mg/g represented 5.4% (n = 129) in men and 7.1% (n = 203) in women (p = 0.027).

Distribution of renal function categories depending on alcohol consumption

We classified eGFR and urine ACR values into three categories. In men and women, heavy drinkers had a higher prevalence of GFR ≥ 90 mL/min/1.73 m², whereas abstainers had a higher prevalence of < 60 mL/min/1.73 m² than others (p = 0.001 for men, p < 0.001 for women). The prevalence of urine ACR values according to the classification of mean daily alcohol intake did not differ in men (p = 0.994), while women heavy drinkers had a higher prevalence of ACR < 30 mg/g than non- and moderate drinkers (p < 0.001; Fig. 1). Regarding binge drinking, in men and women, the prevalence of GFR ≥ 90 mL/min/1.73 m² was higher in binge drinkers than in abstainers or non-binge drinkers (p < 0.001 for men and women). In male binge drinkers, the prevalence of urine ACR ≥ 300 mg/g tended to be lower than in the other groups (p = 0.055), and the trend was similar in women (p < 0.001; Fig. 2).

Mean values of eGFR and urine ACR in participants categorised based on alcohol consumption

After adjusting for age, smoking status, amount of physical activity, morbid state of hypertension, diabetes, dyslipidaemia, anaemia, and BMI, there was a difference in mean eGFR values among non- (89.3 mL/min/1.73 m²), moderate (89.7 mL/min/1.73 m²), and

Table 1. Clinical and laboratory characteristics of the study population

	Men (n=2,386)	Women (n=2,865)	p value
Mean daily alcohol intake, %			<0.001
Abstinence	12.3	33.1	
Moderate drinking	77.1	61.5	
Heavy drinking	10.6	5.3	
Binge drinking status, %			<0.001
Abstinence	12.3	33.1	
Non-binge drinking	13.6	29.3	
Binge drinking	74.1	37.6	
Age (years)	44.1 (0.5)	47.4 (0.5)	<0.001
Current smoker, %	46.3	6.4	<0.001
Sufficient physical activity, %	23.1	17.2	<0.001
BMI(kg/m ²)	24.1 (0.1)	23.4 (0.1)	<0.001
Hypertension, %	29.0	24.1	<0.001
Diabetes mellitus, %	11.7	9.5	0.014
Dyslipidaemia, %	11.1	14.2	0.016
Anaemia, %	2.6	12.0	<0.001
SBP (mmHg)	119.9 (0.4)	115.5 (0.4)	<0.001
DBP (mmHg)	79.1(0.3)	73.5 (0.2)	<0.001
Fasting glucose (mg/dL)	98.6 (0.6)	94.5 (0.4)	<0.001
Total cholesterol (mg/dL)	188.0 (1.1)	190.9(0.8)	0.034
Hemoglobin (g/dL)	15.4 (0.03)	13.1 (0.03)	<0.001
eGFR (mL/min/1.73m ²)	92.8 (0.5)	96.3 (0.5)	<0.001
urine ACR (mg/g)*	4.6 (4.3-4.9)	3.9 (3.6-4.1)	<0.001
eGFR<60 mL/min/1.73m ² , %	1.9	1.7	0.588
urine ACR ≥30 mg/g, %	5.4	7.1	0.027

Values are means (standard error) or percents, and geometric means and 95% confidence intervals for skewed distributions*. BMI = body mass index; SBP = systolic blood pressure; DBP = diastolic blood pressure; eGFR = estimated glomerular filtration rate; urine ACR = urine albumin to creatinine ratio

Fig. 1. Distribution of eGFR (A) and urine ACR categories (B) on renal function depending on mean daily alcohol intake (*p < 0.01).

Fig. 2. Distribution of eGFR (A) and urine ACR categories (B) on renal function depending on binge drinking (*p < 0.01).

Table 2. Adjusted mean values of eGFR and urine ACR according to alcohol consumption	eGFR		urine ACR*	
	Men	Women	Men	Women
Mean daily alcohol intake				
Abstinence	89.3 (1.0)	94.0 (0.8)	4.3(3.7-5.0)	5.3(4.8-5.9)
Moderate drinking	89.7 (0.5)	93.4 (0.6)	4.3(4.0-4.6)	4.7(4.3-5.0)
Heavy drinking	93.0 (1.4)	94.5 (1.4)	4.3(3.6-5.2)	4.5(3.7-5.6)
p value for trend	0.030	0.775	0.995	0.030
Binge drinking status				
Abstinence	89.3 (1.0)	94.0 (0.8)	4.3(3.7-5.1)	5.3(4.8-5.9)
Non-binge drinking	87.8 (1.0)	93.0 (0.7)	4.3(3.9-4.7)	4.5(4.1-5.0)
Binge drinking	90.7 (0.5)	94.0 (0.8)	4.4(4.0-4.7)	4.8(4.4-5.2)
p value for trend	0.057	0.974	0.846	0.073

Values are given as means (standard error) or geometric means and 95% confidence intervals for skewed distribution*. eGFR = estimated glomerular filtration rate; urine ACR = urine albumin to creatinine ratio

heavy drinkers (93.0 mL/min/1.73 m²) in men (p = 0.030), and in mean urine ACR values among non-, moderate, and heavy drinkers in women (5.3, 4.7, and 4.5 mg/g, respectively; p = 0.030; Table 2).

Correlation between renal dysfunction and alcohol consumption

In men, the amount of mean daily alcohol intake and binge-drinking status showed significant trends in the association, with a likelihood of reduced eGFR value (eGFR < 60 mL/min/1.73 m²; p = 0.041 and p = 0.038, respectively). After adjusting for the same covariables as above, in men, heavy drinking was inversely associated with a decrease in renal function,

Table 3. Multivariable-adjusted odds ratios (95% confidence intervals) of prevalence of renal dysfunction according to alcohol consumption

	eGFR <60 mL/min/1.73m ²		ACR >30mg/g	
	Men	Women	Men	women
Mean daily alcohol intake				
Abstinence	1	1	1	1
Moderate drinking	0.76 (0.37,1.59)	0.77 (0.36,1.64)	0.81 (0.48,1.34)	1.04 (0.72,1.51)
Heavy drinking	0.14 (0.01,0.91)	-	1.09 (0.54,2.25)	1.23 (0.35,4.03)
p value for trend	0.041	0.387	0.463	0.837
Binge drinking status				
Abstinence	1	1	1	1
Non binge drinking	1.33 (0.59,2.96)	0.85 (0.38,1.92)	0.88 (0.47,1.66)	1.14 (0.77,1.70)
Binge drinking	0.42 (0.17,0.98)	0.45 (0.13,1.50)	0.76 (0.44,1.30)	0.91 (0.55,1.51)
p value for trend	0.038	0.264	0.262	0.750

eGFR = estimated glomerular filtration rate; urine ACR = urine albumin to creatinine ratio

indicated a reduced eGFR value, than abstinence (adjusted odds ratio = 0.14, 95% CI 0.01-0.91), and the adjusted odds ratio of the reduced eGFR value was 0.42 (95% CI 0.17-0.98) in binge drinking compared with abstinence. There was no association between alcohol consumption and urine ACR in men, or between alcohol consumption and renal dysfunction in women. An analysis for heavy drinking and reduced eGFR value in women was not possible due to low numbers of cases (Table 3).

Discussion

In this study, we investigated the relationship between alcohol consumption and renal dysfunction in the general Korean population. We discovered that in men, the eGFR value was increased as the average amount of daily alcohol intake increased, and heavy drinking and binge drinking were inversely associated with a reduction in eGFR even after adjusting for age, smoking status, amount of physical activity, morbid state of hypertension, diabetes, dyslipidaemia, anaemia, and BMI. However, in women, there was no significant association between alcohol consumption and renal dysfunction.

It has been debated whether alcohol consumption results in renal dysfunction. To date, few epidemiological studies have examined the relationships between alcohol consumption and renal function. Some studies have shown only detrimental effects of alcohol consumption on renal function [15, 16]. However, similar to the results of this study, several studies have shown that alcohol consumption may have positive effects or no association with renal function. Hsu et al. [14] reported an inverse relationship between alcohol consumption and stage 3 chronic kidney disease (CKD) in 11,900 Taiwanese men, but not in 15,353 Taiwanese women. In addition, Schaeffner et al. [10] showed that the amount of alcohol consumption was inversely associated with the risk of reduced eGFR over 14.2 years of follow-up in a prospective cohort study of 11,023 men, and Funakoshi et al. [13] found an inverse association between frequency of alcohol consumption and CKD in 9,196 men. Similarly, in a prospective cohort of 65,601 Chinese men age 40 years and older, there was an inverse association between alcohol consumption and the incidence of end-stage renal disease [12] whereas in a prospective study of 1,658 women aged 30-55 years [17] and in a community-based longitudinal study of 4,343 elderly adults aged ≥ 65 years [18], there was no association between the amount of alcohol intake and decline in renal function. Furthermore, in a cross-sectional community-based study of 1,466 men and women aged 50-95 years, as the amount of alcohol consumption was increased, the values of eGFR and creatinine clearance rates increased [11].

We hypothesised that moderate and non-binge alcohol drinking would be positively associated with renal function whereas heavy or binge drinking would have adverse effects on renal function. However, we found a positive association between renal function and heavy drinking as well as binge drinking in men, but not in women. The mechanisms that link alcohol consumption to cardiovascular risks [32] could involve a mechanism between alcohol consumption and renal dysfunction. Indeed, the effects of alcohol on cardiovascular outcomes are complex and multidimensional. Depending on amount of alcohol intake and drinking pattern, the cardiovascular results differ, which has been attributed to mixed effects of the beneficial and detrimental effects of alcohol on lipid profile, glucose metabolism, and haemostatic factors [22]. However, the protective effects of alcohol consumption, mediated by an increase in high-density lipoprotein cholesterol levels [33, 34] and insulin sensitivity [35], and a decrease in platelet aggregation and fibrinolytic activity [33, 34] may affect renal function favourably in men.

Because not only the average amount of alcohol intake but also drinking patterns provide important information about the risks of drinking alcohol [21-23], the drinking pattern needs to be considered and evaluated in the influence of alcohol consumption on renal function. However, to our knowledge, no reported study has examined the relationship between renal function and drinking pattern, especially binge drinking. Thus, we examined the effects of the amount of alcohol intake as well as binge drinking on renal function. Notwithstanding that binge drinking has more harmful effects on physiological status than heavy drinking [21, 22, 24], in this study, binge drinking, similar to heavy drinking, was inversely associated with the prevalence of renal dysfunction.

In this study, the effects of alcohol consumption on renal function differed between men and women. In contrast with the positive relationship between alcohol consumption and eGFR in men, there was no association between alcohol consumption and renal function in women. A potential explanation is that women are less able to metabolise alcohol than men, due to gender-related differences in lean body mass, body fat, total body fluid, and activity of the alcohol-processing enzymes in liver [36], suggesting that any favourable effect of alcohol consumption on renal function may be attenuated.

The development of CKD has been associated with increased age [37], and the age might have affected the results of this study. Therefore, we performed additional sub-group analysis for the results of the association of alcohol consumption and a likelihood of renal insufficiency regarding the age: < 65 and ≥ 65 years. Of study participants, 13.7% (11.1% of men, 16.5% of women) was those aged 65 years and older. The sub-group analysis of the association between the amount of mean daily alcohol intake, binge-drinking status and the reduced eGFR value in men aged 65 years and older showed an inverse association (for the amount of mean daily alcohol intake: moderate drinking, adjusted odds ratio = 0.59, 95% CI 0.30-1.14, heavy drinking, adjusted odds ratio = 0.29, 95% CI 0.03-1.73, and for binge-drinking status: non-binge drinking, adjusted odds ratio = 1.09, 95% CI 0.50-2.38, binge drinking, adjusted odds ratio = 0.24, 95% CI 0.10-0.57) and the p values for trend were significant (for the amount of mean daily alcohol intake, $p = 0.044$, and for binge-drinking status, $p < 0.001$). The sub-group analysis of the association between the amount of mean daily alcohol intake and the reduced eGFR value in men younger than 65 years was not possible due to low numbers of cases, and the association between binge-drinking status and the reduced eGFR value in men younger than 65 years was disappeared in the sub-group analysis ($p = 0.579$). The sub-group analyses of the associations between alcohol consumption and urine ACR in men, or between alcohol consumption and renal dysfunction in women showed no significant results.

The strength of this study is that the data collected through a representative nationwide survey of the South Korean population were used for this study and that this is the first, to our knowledge, to investigate the relationship between the amount and pattern of alcohol consumption and the renal dysfunction, which was measured using both eGFR and urine ACR. However, this study has some limitations. First, this study was conducted under the

cross-sectional design. Second, there was the probability of recall bias from a self-reporting questionnaire survey. Third, several epidemiologic studies have been suggested an associate between the development of CKD and increased uric acid level among general population [38]. However, in the KNHANES, serum uric acid levels have not been measured, so we could not consider it to covariate. Fourth, we used GFR estimation with the MDRD study equation using serum creatinine levels for evaluating renal function. In fact, serum creatinine is affected by a number of factors, such as diet, malnutrition, and muscle wasting, which may be related to alcohol consumption [39], so that it could induce some degree of measurement bias in eGFR. Additionally, albuminuria may be an early marker of renal dysfunction, independently of eGFR [28, 40], however, there was a critical measurement issue that the ascertainment of albuminuria as urine ACR was made at a single point in time [29]. The spot urine ACR could be one of the screening test, but not a diagnostic test for albuminuria [41, 42], due to the influence by the urine creatinine concentration and by the total daily creatinine production, and the variation of the urine protein excretion throughout the day or from day to day [43]. Considering the vulnerability of urine ACR levels using the spot urine, further studies are warranted to clarify the association between alcohol drinking and albuminuria.

Conclusion

Alcohol consumption was inversely associated with a reduction in eGFR in Korean men, but in women, alcohol drinking had no association with the eGFR value, and in both men and women there was no association between alcohol consumption and urine ACR. However, heavy alcohol consumption or binge drinking may lead to increases in other chronic diseases and social problems, such as accidents, intentional injuries or deaths, and violence [44]. Thus, our results should be considered cautiously, given the other harmful effects related to alcohol consumption. Further investigations are warranted to confirm the association reported here and to examine the possible mechanisms.

Disclosure Statement

The authors of this manuscript state that they do not have any conflict of interests and nothing to disclose.

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