ORIGINAL ARTICLE

Association of alcohol consumption with the prevalence and various stages of chronic kidney disease

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Background: Considering that the effect of alcohol consumption trend on the prevalence of kidney damage and its progression has not been determined yet, the study aimed at investigating the association between alcohol consumption and the risk of chronic kidney disease (CKD) prevalence and progression at various stages of the disease. **Materials and Methods:** This cross-sectional study was performed on 3374 participants that referred to health-care centers in Isfahan from 2017 to 2019. Participants' basic and clinical characteristics (such as sex, age, education level, marital status, body mass index, blood pressure, alcohol consumption, comorbidities, and laboratory parameters) were evaluated and recorded. The alcohol consumption trend was classified as never, occasional (<6 drinks/week), and frequent (≥6 drinks/week) based on the amount of alcohol consumption over the last 3 months. Moreover, CKD stages were recorded based on the Kidney Disease: Improving Global Outcomes guideline, as well. **Results:** In the present study, the occasional and frequent drinking of alcohol did not have a significant effect on the odds of CKD prevalence (odds ratio [OR]: 1.32 and 0.54; $P > 0.05$) and the odds of stage 2 CKD prevalence as compared to stage 1 CKD prevalence (OR: 0.93 and 0.47; $P > 0.05$). However, adjusting the confounding factors revealed that occasional drinking as compared to nondrinking increased the odds of stage 3 and 4 CKD prevalence as compared to stage 1 CKD prevalence by 3.35 folds, respectively ($P < 0.05$). **Conclusion:** According to the results of this study, occasional drinking as compared to nondrinking significantly increased the odds of stage 3 and 4 CKD prevalence as compared to stage 1 CKD prevalence.

Key words: Alcohol drinking, chronic kidney disease, glomerular filtration rate

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INTRODUCTION

Chronic kidney disease (CKD) refers to kidney dysfunction lasting for more than 3 months. Several different stages have been defined for this disease. CKD is one of the most common diseases in the world, and 288 million individuals suffer from this disease worldwide.[1] CKD is not only a major public health concern due to the increased risk of cardiovascular disease and mortality, its significant economic burden, the development of various mental and physical problems such as depression and physical disabilities for the patients and their families, and the patients' poor quality of life but also has created a significant disease burden imposed on society.[2,3] Therefore, the early detection of factors increasing or decreasing the risk of CKD can help reduce the disease burden.[3]

Considering that the progression of CKD can be prevented by controlling some modifiable risk factors such as blood pressure, cardiovascular events, blood sugar, nephrotoxic drugs, obesity, and salt intake,[4-6]

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it seems essential to pay due attention to the potential risk factors in this regard to prevent the development of CKD. In this regard, excessive or prolonged alcohol consumption as one of the most common psychedelics in the world is considered a potential risk factor for cardiovascular diseases such as hypertension (HTN) and cerebrovascular accidents.[7,8]

Moreover, excessive alcohol consumption is also associated with liver diseases, HTN, cardiac arrhythmias, epilepsy, poisoning, motor vehicle accidents, violence, and various types of cancers.[7,9] Another clinical study has indicated that the amount and trend of alcohol consumption both affect estimated glomerular filtration rate (eGFR) in patients with CKD.[10,11]

It seems that the alcohol consumption trend is a significant factor affecting CKD in these patients. Contrary to empirical studies, the alcohol consumption trend in humans is very imprecise, and the major question of whether occasional, frequent, and excessive drinking statuses cause kidney failure and progression of kidney diseases has remained unanswered.

There is limited research addressing the association between the alcohol consumption trend and different CKD stages. In addition, most studies focusing on the association of alcohol consumption with kidney disease have not controlled the confounding variables such as anemia, smoking, cardiovascular disease, and HTN, which raises concerns about the validity of the reported association.

For this purpose, the present study in the first step presented the alcohol consumption trend and compared other basic and clinical characteristics among individuals with and without CKD and in the second step investigated the association of alcohol consumption with the prevalence of CKD and the progression of different stages of CKD by controlling the confounding variables.

SUBJECTS AND METHODS

Study design and subjects

This study was a cross-sectional study. According to the report provided by the National Organization for Civil Registration of Iran, 2,243,249 individuals were referred to all health-care centers in Isfahan from 2017 to 2019. The sample size of this study included 3374 individuals that were selected from the mentioned population at 95% confidence interval, the test power of 80%, and considering the prevalence of CKD reported in recent studies[4] conducted in our country equal to 6%, and the error level of 0.008.

Sampling procedure

The sample was selected using a multi-stage cluster random sampling method. To do this, each city district was considered a cluster based on the health-care system coverage. In the first stage, 10 city districts were selected. In the second stage, 3–4 units were randomly selected from each city district according to the latest population statistics report. In the third stage, some individuals covered by the health-care system of those units were randomly selected.

Study participants

Inclusion criteria consisted of adults who were living in Isfahan and were registering in health centers and referred as routine clinical and laboratory evaluations, were 18-year-old and more, had no common cold and fever at the time of performing laboratory tests, agreed to participate in the study, were fasting, and did not perform heavy exercises over the last 48 h before performing laboratory tests. Moreover, the subjects who had incomplete checklists, were pregnant, or were in their menstruation period were excluded from the study.

Data collection procedure

After obtaining the code of ethics from Isfahan University of Medical Sciences (approval code: IR. MUI. REC.1396.1.086) and obtaining the written consent from eligible individuals, all subjects underwent laboratory tests and filled out checklists regarding their past medical history with the help of a trained researcher. The following question was used to specify the patients' alcohol consumption trend: "How many times have you drunk alcohol or alcohol-containing beverages over the last 3 months?, which had the following choices: not at all, occasionally (<6 drinks/week), and frequently (≥6 drinks/week)."[9]

Therefore, according to the provided responses by the subjects and regardless of the amount of their alcohol consumption, they were categorized as nondrinkers in case of not consuming alcohol over the last 3 months, <6 drinks/week in case of consuming alcohol occasionally, and equal and higher than 6 drinks/week in case of consuming alcohol regularly or frequently.[9]

Based on subjects' response to the mentioned question, subjects were classified into nondrinkers, occasional drinkers, or frequent drinkers, respectively. Subjects' demographic and clinical characteristics including age, sex, body mass index (BMI), marital status, employment status, smoking status and type of smoking, alcohol consumption, systolic blood pressure, diastolic blood pressure, serum creatinine, total cholesterol (TC), low-density lipoprotein (LDL), high-density lipoprotein (HDL), triglyceride, fasting blood glucose, microalbumin, albumin-to-creatinine ratio (ACR), use of drugs such as nonsteroidal anti-inflammatory,

angiotensin-converting-enzyme inhibitors, angiotensin receptor blockers, calcium channel blockers, beta-blocker, diuretics, antidiabetic drugs, and antihyperlipidemic agents, and personal medical history including CKD, diabetes mellitus (DM), HTN, cardiovascular disease, hyperlipidemia, hyperuricemia, and anemia were obtained and recorded. Categories of normal, moderately increased albuminuria, and severely increased albuminuria were assigned to patients with ACR determinations of <30, 30–299, and higher than 300 mg/g, respectively. Moreover, double check was performed for all patients with ACR >30 mg/g. The CKD-Epidemiology Collaboration equation presented in the Modification of Diet in Renal Disease study was used to calculate eGFR.[12,13]

Definitions

The Kidney Disease: Improving Global Outcomes guideline was used to define the CKD stages. Stage 1 CKD was defined by the eGFR value of equal to or >90 mL/min/1.73 m^2 along with the evidence of kidney damage. Stage 2 CKD was characterized by the eGFR value range of 60–89 mL/min/1.73 m^2 along with the evidence of kidney damage. Moreover, stage 3 CKD was specified by the eGFR value range of 30–59 mL/min/1.73 m^2. Furthermore, the eGFR between 15 and 29 mL/min/1.73 m^2 was considered a severe decrease in GFR and stage 4 CKD. Finally, the eGFR <15 mL/min/1.73 m^2 (dialysis dependent; kidney failure) was regarded as stage 5 CKD.[12]

Proteinuria was defined as + 1 to + 4 in a morning urine dipstick test. HTN was defined as the definite history of HTN confirmed by a health-care professional or as the blood pressure of above 140/90 mmHg (regardless of medication). DM was defined as the fasting plasma glucose level of at least 126 mg/dL or a history of DM confirmed by a health-care professional (regardless of medication). Hyperlipidemia was defined as the serum TC level of above 200 mg/dL, the TG level of at least 200 mg/dL, or a history of disease confirmed by a health-care professional (with or without medication). Anemia was defined as the Hb level of <13 g/dL in men and <12 g/dL in nonpregnant women. Hyperuricemia was defined as the serum UA level of >7.0 mg/dL.[14]

It is necessary to mention, to identify the patients, either the mentioned tests were used or patient records were checked for the history of these diseases.

Statistical analysis

The collected data were entered into SPSS software (version 25, IBM Corporation, Armonk, NY). Quantitative variables were shown as means ± standard deviation and qualitative variables as frequency (%). The Chi-square test, independent samples *t*-test, and one-way analysis of variance were used to compare the frequency distribution of qualitative data and the mean of quantitative data among alcohol consumption trends or between two groups of CKD and non-CKD, respectively. Binary logistic regression analysis was used to evaluate the association between the CKD prevalence (CKD vs. non-CKD) and alcohol consumption trend (not at all, occasionally, and frequently) and other confounding factors. In addition, multinomial logistic regression analysis was used to evaluate the association between different stages of CKD with alcohol consumption trend and other confounding factors. In this analysis, stage 1 CKD was considered a reference (the odds of stage 2 CKD prevalence versus stage 1 CKD prevalence and the odds of stage 3 and 4 CKD prevalence versus stage 1 CKD prevalence). In both regression analyses, alcohol consumption trend was evaluated with and without confounding factors (models 1 and 2). The odds ratio (OR) values were reported with a 95% confidence interval (CI). The significance level of less than 0.05 was considered in all analyses.

RESULTS

In this study, out of 3374 participants, 1374 (40.7%) were female and 2000 (59.3%) were male with a mean age of 49.30 ± 14.09 years and a mean eGFR of 89.31 ± 19.66 mL/min/1.73 m2. Moreover, 636 (18.9%) and 2738 (81.1%) individuals had and did not have CKD, respectively. Of the individuals with CKD, 38.4%, 40.7%, 19.5%, and 1.4% were in stages 1, 2, 3, and 4, respectively. In addition, 3278 individuals did not consume any alcohol, 34 had occasional alcohol consumption, and 62 had frequent alcohol consumption. The analysis of demographic and clinical characteristics was provided based on the alcohol consumption trend and the CKD and non-CKD categorization in Tables 1 and 2, respectively.

Examining the factors related to the CKD prevalence showed that the alcohol consumption in an occasional drinking or frequent drinking did not have a significant relationship with the CKD prevalence (*P* value >0.05). In addition, by adjusting the confounding factors (model 2), it was found that patients' age (OR: 1.69; $P = 0.013$), sex (OR: 1.92; $P < 0.001$), Cr (OR: 18.74; *P* value <0.001), microalbumin (OR: 1.03; $P < 0.001$), ACR (OR: 1.07; *P* value <0.001), and hematuria (OR: 2.89; $P < 0.001$) significantly increased the odds of CKD, while HDL (OR: 0.98; $P = 0.037$) reduced the odds of CKD [Table 3].

Furthermore, examining the factors related to the prevalence of different severities of CKD showed that the alcohol consumption in an occasional drinking or frequent drinking had no significant relationship with increasing the odds of stage 2 CKD compared to stage 1 CKD ($P > 0.05$). On the other

Table 1: Demographic and clinical characteristics of chronic kidney disease patients based on patients' alcohol consumption

Variables	Overall (*n*=3374), *n* (%)	Non (*n*=3278), *n* (%)	Occasionally (*n*=34), *n* (%)	Frequent (*n*=62), *n* (%)	*P*
Sex					
Female	1374 (40.7)	1289 (39.3)	29 (85.3)	56 (90.3)	<0.001†
Male	2000 (59.3)	1989 (60.7)	5 (14.7)	6 (9.7)	
Age (years)	49.30±14.09	49.40±14.09	50.29±12.60	43.47±13.93	0.004††
≤50	1784 (52.9)	1722 (52.5)	17 (50)	45 (72.6)	0.007†
>50	1590 (47.1)	1556 (47.5)	17 (50)	17 (27.4)	
Education level					
Middle school or lower	450 (13.3)	448 (13.7)	1 (2.9)	1 (1.6)	0.009†
High school	2276 (67.4)	2198 (67.0)	30 (88.3)	48 (77.4)	
College or higher	648 (19.2)	632 (19.3)	3 (8.8)	13 (21)	
Marital status					
Single	306 (9.1)	292 (8.9)	1 (2.9)	13 (21.0)	0.013†
Married	2884 (85.5)	2804 (85.5)	33 (97.1)	47 (75.8)	
Widow	158 (4.7)	157 (4.8)	0	1 (1.6)	
Divorced	26 (0.8)	25 (0.8)	0	1 (1.6)	
BMI (kg/m2)	26.90±4.51	26.92±4.50	26.95±5.36	25.96±4.78	0.251††
SBP (mmHg)	121.08±19.34	120.95±19.28	126.97±17.15	124.74±22.71	0.063††
DBP (mmHg)	78.14±11.56	78.07±11.53	81.86±10.04	79.99±13.56	0.073††
Smoking					
Cigarette	295 (8.7)	249 (7.6)	17 (50.0)	29 (46.8)	<0.001†
Pipe	5 (0.1)	2 (0.1)	2 (5.9)	1 (1.6)	<0.001†
hookah	223 (6.6)	199 (6.1)	6 (17.6)	18 (29.0)	<0.001†
Others	15 (0.4)	22 (0.7)	5 (14.7)	4 (6.4)	0.036†
Comorbidities					
Diabetes mellitus	450 (13.3)	441 (13.5)	5 (14.7)	4 (6.5)	0.268†
Hypertension	1565 (46.4)	1529 (46.6)	13 (38.2)	23 (37.1)	0.207†
Cardiovascular disease	951 (28.2)	932 (28.4)	8 (23.5)	11 (17.7)	0.149†
Cerebrovascular disease	699 (20.7)	690 (21.0)	5 (14.7)	4 (6.5)	0.013†
Hyperlipidemia	1021 (30.3)	1004 (30.6)	6 (17.6)	11 (17.7)	0.025†
Gout	23 (0.7)	22 (0.7)	1 (2.9)	0	0.224†
Anemia	466 (13.8)	462 (14.1)	3 (8.8)	1 (1.6)	0.013†
Musculoskeletal disease	311 (9.2)	307 (9.4)	1 (2.9)	3 (4.8)	0.212†
Hypotension	81 (2.4)	77 (2.3)	0	4 (6.5)	0.074†
Kidney stone	554 (16.4)	538 (16.4)	8 (23.5)	8 (12.9)	0.404†
Hematuria	105 (3.1)	104 (3.2)	1 (2.9)	0	0.362†
Proteinuria	55 (1.6)	54 (1.6)	1 (2.9)	0	0.497†
Hepatitis	5 (0.1)	5 (0.2)	0	0	0.929†
CKD stage					
Non-CKD	2738 (81.1)	2657 (81.1)	26 (76.5)	55 (88.7)	
Stage 1	244 (7.2)	237 (7.2)	3 (8.8)	4 (6.5)	0.012†
Stage 2	259 (7.7)	254 (7.8)	3 (8.8)	2 (3.2)	
Stage 3	124 (3.7)	122 (3.7)	2 (5.9)	0	
Stage 4	9 (0.3)	8 (0.2)	0	1 (1.6)	
Laboratory parameters					
Creatinine (mg/dL)	1.01±0.09	1.01±0.09	1.00±0.01	1.02±0.13	0.696††
Microalbumin (mg)	24.09±75.86	23.51±66.97	23.47±28.77	25.42±27.47	0.078††
ACR	26.77±16.40	26.78±16.24	21.35±16.61	29.44±13.01	0.974††
FBG (mg/dL)	90.22±27.56	90.28±27.67	88.29±30.76	86.60±20.99	0.536††
Cholesterol (mg/dL)	171.47±49.66	171.43±49.57	165.44±44.94	177.05±56.47	0.526††
TG (mg/dL)	154.32±68.84	153.91±68.42	170.29±92.12	167.23±75.05	0.127††
LDL (mg/dL)	96.47±30.49	96.58±30.54	90.54±26.51	93.85±29.95	0.410††
HDL (mg/dL)	51.00±11.05	51.10±11.07	45.26±9.15	49.16±9.86	0.400††

Contd...

Table 1: Contd...

Variables	Overall (*n*=3374), *n* (%)	Non (*n*=3278), *n* (%)	Occasionally (*n*=34), *n* (%)	Frequent (*n*=62), *n* (%)	*P*
Drugs					
NSAID	227 (6.7)	225 (6.8)	1 (2.9)	1 (1.6)	0.536†
ACEI	25 (0.7)	25 (0.8)	0	0	0.692†
ARB	486 (14.4)	475 (14.5)	4 (11.8)	7 (11.3)	0.705†
CCB	37 (1.1)	36 (1.1)	0	1 (1.6)	0.767†
Beta-blocker	94 (2.8)	94 (2.9)	0	0	0.243†
Diuretics	60 (1.8)	59 (1.8)	0	1 (1.6)	0.728†
Antidiabetic drugs	591 (17.5)	581 (17.7)	7 (20.6)	3 (4.8)	0.104†
Antihyperlipidemic agents	645 (19.1)	636 (19.4)	6 (17.6)	3 (4.8)	0.015†

†The significance level of Chi-square test to compare the frequency distribution of qualitative variables between alcohol consumption trends; ††The significance level of one-way ANOVA to compare the mean of quantitative variables between alcohol consumption trends. ACR=Albumin-to-creatinine ratio; FBG=Fasting blood glucose; TG=Triglyceride; LDL=Low-density lipoprotein; HDL=High-density lipoprotein; NSAID=Nonsteroidal anti-inflammatory drug; ACEI=Angiotensin-converting enzyme inhibitor; ARB=Angiotensin receptor blocker; CCB=Calcium channel blocker; BMI=Body mass index; BP=Blood pressure; SBP=Systolic BP; DBP=Diastolic BP; ANOVA=Analysis of variance; CKD=Chronic kidney disease

hand, by adjusting the confounding factors (model 2), it was observed that the age over 50 years (OR: 6.74; $P < 0.001$), increased LDL (OR: 1.01; $P = 0.013$), and cerebrovascular disease (OR: 3.24; $P = 0.002$) increased the odds of stage 2 CKD compared to stage 1 CKD ($P > 0.05$). In addition, although the odds of stage 3 and 4 CKD compared to stage 1 CKD did not change with alcohol consumption without adjusting the confounding factors (model 1) ($P > 0.05$), occasional drinking alcohol consumption increased the odds of stage 3 and 4 CKD compared to stage 1 CKD by 3.35 folds by adjusting the confounding factors (model 2). Moreover, the age over 50 years (OR: 6.12; $P < 0.001$) and Cr (OR: 3.39; P value = 0.040) also increased the odds of increasing the severity of CKD from stages 3 and 4 to stage 1; however, increasing DBP (OR: 0.94; $P = 0.007$) and HDL (OR: 0.95; $P = 0.018$) reduced this odds [Table 4].

DISCUSSION

According to the results of the study, out of 3374 participants, 81.1% had no CKD and 18.9% had CKD. Moreover, 38.4%, 40.7%, 19.5%, and 1.4% of patients with CKD were in stages 1, 2, 3, and 4, respectively. In addition, 3278, 34, and 62 individuals had no, occasional, and frequent alcohol consumption, respectively.

Considering that unhealthy behaviors among alcoholics can be a risk factor for increasing the odds of developing CKD, it seems that evaluating the association between alcohol consumption and CKD prevalence and severity is very significant. In fact, according to previous reports, alcohol consumption is a factor that may interfere with the prognosis of CKD. Another array of studies has indicated that alcohol consumption along with energy drinks, caffeine, or soft drinks can disrupt the physiological redox reaction and cause lipoperoxidation in the liver and poisoning in kidney.[15-18] Hence, it seems that the protective effects can lead to confound in assessing the association between alcohol consumption and the prevalence of CKD and its severity.

Therefore, this study adjusted the role of confounding factors along with alcohol consumption so that it was possible to more confidently and accurately assess the possible association between alcohol consumption trends and the CKD prevalence as well as various CKD stages.

According to the results of this study, although the odds of CKD prevalence was higher at older ages (>50 years) and in men, with a history of hematuria, increased HDL, and Cr, its prevalence was not significantly associated with alcohol consumption.

Examining the association between alcohol consumption and the severity of this disease revealed that the alcohol consumption trend had no significant effect on the odds of stage 2 CKD prevalence as compared to stage 1 CKD prevalence in all three evaluated models ($P > 0.05$). Rather, the odds of stage 2 CKD prevalence as compared to stage 1 CKD prevalence had a positive and significant association with patients' age, increased LDL, and history of cerebrovascular disease. It should be noted that as the number of patients with stage 3 and 4 CKD was low, these two stages were considered together. Moreover, the findings indicated that occasional drinking as compared to nondrinking has increased the odds of stage 3 and 4 CKD prevalence as compared to stage 1 CKD prevalence by 3.35 folds (model 2) by adjusting the confounding factors ($P < 0.05$). Furthermore, aging and Cr were positively associated while DBP and HDL were negatively associated with stage 3 and 4 CKD prevalence compared to stage 1 CKD prevalence.

In this regard, Joo *et al*. revealed that excessive alcohol consumption was associated with the faster progression of CKD. They also stated that there was a particularly

Table 2: Comparison of demographic and clinical characteristics of patients between chronic kidney disease and nonchronic kidney disease

Variables	CKD (*n*=636)				Non-CKD (*n*=2738)	*P*[a]	*P*[b]
	Overall (*n*=636)	Stage 1 (*n*=244)	Stage 2 (*n*=259)	Stage 3, 4 (*n*=133)			
Sex							
Female	224 (35.2)	74 (30.3)	91 (35.1)	59 (44.4)	1150 (42.0)	0.002†	0.024†
Male	412 (64.8)	170 (69.7)	168 (64.9)	74 (55.6)	1588 (58.0)		
Age (year)	53.96±15.60	42.03±11.31	58.32±13.16	67.32±10.81	48.22±13.50	0.003††	<0.001††
≤50	262 (41.2)	186 (76.2)	70 (27.0)	6 (4.5)	1522 (55.6)	<0.001†	<0.001†
>50	374 (58.8)	58 (23.8)	189 (73.0)	127 (95.5)	1216 (44.4)		
Education level							
Middle school or lower	134 (21.1)	17 (7.0)	66 (25.5)	51 (38.3)	316 (11.5)	<0.001†	
High school	409 (64.3)	165 (67.6)	171 (66.0)	73 (54.9)	1867 (68.2)		<0.001†
College or higher	93 (14.6)	62 (25.4)	22 (8.5)	9 (6.8)	555 (20.3)		
Marital status							
Single	43 (6.8)	28 (11.5)	12 (4.6)	3 (2.3)	263 (9.6)	<0.001†	<0.001†
Married	524 (82.4)	209 (85.7)	212 (81.9)	103 (77.4)	2360 (86.2)		
Widow	64 (10.1)	4 (1.6)	33 (12.7)	27 (20.3)	94 (3.4)		
Divorced	5 (0.8)	3 (1.2)	2 (0.8)	0	21 (0.8)		
BMI (kg/m^2)	27.48±4.84	26.83±5.22	27.78±4.56	28.09±4.58	26.76±4.42	0.001††	0.023††
SBP (mmHg)	126.40±22.54	117.91±19.93	129.95±22.09	135.07±22.94	119.85±18.30	<0.001††	<0.001††
DBP (mmHg)	79.84±12.74	77.49±12.20	81.50±12.53	80.94±13.52	77.74±11.24	<0.001††	0.001††
Smoking							
Cigarette	40 (6.3)	11 (4.5)	23 (8.9)	6 (4.5)	255 (9.3)	0.115†	0.083†
Pipe	1 (0.2)	1 (0.4)	0	0	4 (0.1)	0.948†	0.447†
Hookah	35 (5.5)	18 (7.4)	11 (4.2)	6 (4.5)	188 (6.9)	0.213†	0.261†
Others	5 (0.8)	3 (1.2)	2 (0.8)	0	10 (0.4)	0.136†	0.163†
Alcohol consumption							
Non	621 (97.6)	237 (97.1)	254 (98.1)	130 (97.7)	2657 (97)	0.044†	0.039†
Occasionally	8 (1.3)	3 (1.2)	3 (1.2)	2 (1.5)	26 (0.9)		
Frequent	7 (1.1)	4 (1.6)	2 (0.8)	1 (0.8)	55 (2.0)		
Comorbidities							
Diabetes mellitus	136 (21.4)	27 (11.1)	61 (23.6)	48 (36.1)	314 (11.5)	<0.001†	<0.001†
Hypertension	294 (46.2)	127 (52.0)	112 (43.2)	55 (41.4)	1271 (46.4)	0.929†	0.063†
Cardiovascular disease	184 (28.9)	77 (31.6)	78 (30.1)	29 (21.8)	767 (28)	0.643†	0.118†
Cerebrovascular disease	174 (27.4)	25 (10.2)	84 (32.4)	65 (48.9)	525 (19.2)	<0.001†	<0.001†
Hyperlipidemia	191 (30)	91 (37.3)	64 (24.7)	36 (27.1)	830 (30.3)	0.889†	0.160†
Gout	8 (1.3)	2 (0.8)	1 (0.4)	5 (3.8)	15 (0.5)	0.061†	0.086†
Anemia	96 (15.1)	36 (14.8)	40 (15.4)	20 (15.0)	370 (13.5)	0.298†	0.977†
Musculoskeletal disease	73 (11.5)	13 (5.3)	37 (14.3)	23 (17.3)	238 (8.7)	0.029†	<0.001†
Hypotension	16 (2.5)	9 (3.7)	4 (1.5)	3 (2.3)	65 (2.4)	0.833†	0.301†
Kidney stone	139 (21.9)	41 (16.8)	68 (26.25)	30 (22.6)	415 (15.2)	<0.001†	0.040†
Hematuria	42 (6.6)	10 (4.1)	22 (8.9)	10 (7.5)	63 (2.3)	<0.001†	0.088†
Proteinuria	24 (3.8)	8 (3.3)	7 (2.7)	9 (6.8)	31 (1.1)	<0.001†	0.019†
Hepatitis	2 (0.3)	0	0	2 (1.5)	3 (0.1)	0.226†	0.230†
Laboratory parameters							
Creatinine (mg/dL)	1.04±0.21	1.00±0.01	1.00±0.01	1.18±0.42	1.01±0.03	<0.001††	<0.001††
Microalbumin; mg	23.51±66.97	70.62±85.74	64.76±20.25	74.34±20.41	23.47±28.77	0.005††	0.045††
ACR	26.78±16.26	61.79±15.38	65.71±15.99	78.02±14.22	21.35±36.61	<0.001††	0.001††
FBG (mg/dL)	97.42±38.25	90.17±29.97	100.63±43.17	104.49±39.66	88.51±24.17	<0.001††	<0.001††
Cholesterol (mg/dL)	171.44±48.42	167.32±46.12	176.67±52.75	168.80±42.80	171.48±49.95	0.983††	0.075††
TG (mg/dL)	155.59±68.95	146.87±71.08	160.38±67.20	162.24±67.16	154.03±68.82	0.607††	0.061††
LDL (mg/dL)	93.53±31.47	89.91±26.37	98.89±33.83	89.71±33.96	97.15±30.22	0.007††	0.002††
HDL (mg/dL)	49.86±10.40	50.58±10.64	50.53±10.80	47.26±8.64	51.27±11.18	0.004††	0.005††

Contd...

Table 2: Contd...

Variables	CKD (*n*=636)				Non-CKD (*n*=2738)	*P*[a]	*P*[b]
	Overall (*n*=636)	Stage 1 (*n*=244)	Stage 2 (*n*=259)	Stage 3, 4 (*n*=133)			
Drugs							
NSAID	49 (7.7)	19 (7.9)	26 (10.0)	4 (3.0)	178 (6.5)	0.503[†]	0.364[†]
ACEI	7 (1.1)	0	3 (1.2)	4 (3)	18 (0.7)	0.240[†]	0.082[†]
ARB	144 (22.6)	22 (9.0)	60 (23.2)	62 (46.6)	342 (12.5)	<0.001[†]	<0.001[†]
CCB	9 (1.4)	1 (0.4)	4 (1.5)	4 (3.0)	28 (1)	0.392[†]	0.121[†]
Beta-blocker	30 (4.7)	8 (3.3)	12 (4.6)	10 (7.5)	64 (2.3)	0.001[†]	0.048[†]
Diuretics	16 (2.5)	4 (1.6)	5 (1.9)	7 (5.3)	44 (1.6)	0.118[†]	0.074[†]
Antidiabetic drugs	192 (30.2)	35 (14.3)	86 (21.6)	71 (53.4)	399 (14.6)	0.314[†]	0.253[†]
Antihyperlipidemic agents	162 (25.5)	23 (9.4)	76 (29.3)	63 (47.4)	483 (17.6)	<0.001[†]	<0.001[†]

[a]*P*: The significance level of comparison of variables between CKD and non-CKD groups; [b]*P*: The significance level of comparing variables among different stages of CKD; [†]The significance level of Chi-square test to compare the frequency distribution of qualitative variables between CKD and non-CKD; [††]The significance level of independent sample *t*-test to compare the mean of quantitative variables between CKD and non-CKD. BP=Blood pressure; SBP=Systolic BP; DBP=Diastolic BP; ACR=Albumin-to-creatinine ratio; FBG=Fasting blood glucose; TG=Triglyceride; LDL=Low-density lipoprotein; HDL=High-density lipoprotein; NSAID=Nonsteroidal anti-inflammatory drugs; ACEI=Angiotensin-converting enzyme inhibitors; ARB=Angiotensin receptor blockers; CCB=Calcium channel blockers; CKD=Chronic kidney disease; BMI=Body mass index

evident association between CKD progression and occasional and regular binge drinking in patients with proteinuria and decreased kidney function. Moreover, a significant interaction was reported between eGFR and alcohol consumption for CKD progression.[9] Another study indicated that four or more drinks a day (especially when accompanied by smoking) was independently associated with an increased risk of CKD in another American population.[19]

In contrast, the results of the study conducted by Hsu *et al*. showed that the prevalence of stage 3 CKD in alcoholics was lower than its prevalence in nonalcoholics and the percentage of alcoholics with stage 3 CKD was lower than nonalcoholics. In addition, higher age, HTN, anemia, BMI of at least 24, hyperuricemia, and proteinuria were also associated with stage 3 CKD in male patients.[20] The mentioned findings should be interpreted with caution given that they have reported an inverse association between alcohol consumption and CKD without adjusting the age, medical history, and other dangerous behaviors.

Moreover, some previous studies have stated that moderate alcohol consumption in patients with CKD not only had no side effects but also was beneficial.[21-23] Moderate alcohol consumption was associated with a reduced risk of CKD in Japanese,[22] Dutch,[23] and Australian[21] adults. The results of their study are inconsistent with our study. In fact, we have shown that alcohol consumption can increase the odds of developing higher levels of CKD. What makes the results of these studies different from our study can be due to the criteria for alcohol consumption, how to determine the amount of alcohol, the culture of that country, and also the lack of consideration of confounding factors.

In addition, there are several potential explanations for the inverse association between alcohol consumption and CKD. The polyphenols in many alcoholic drinks are believed to have beneficial health effects due to their antioxidant properties.[24] Long-term alcohol consumption may reduce kidney damage by inducing catalase, superoxide dismutase, or glutathione peroxidase. Other animal studies have revealed that alcohol can protect against renal ischemia/perfusion injury,[20,24-26] reduce renal arterial hyalinization regardless of its effect on other risk factors of cardiovascular disease,[27] and prevent leukocyte uptake and endothelial barrier damage.[28]

It is worth noting, however, that unfortunately, many of these studies did not provide any accurate information about subjects' kidney function and comorbidities; therefore, their findings should be interpreted with caution. Sick individuals are more likely to reduce or stop drinking alcohol while healthy individuals are more likely to drink alcohol regularly. Consequently, the results may be biased toward the positive effects of alcohol on clinical outcomes. Given the mentioned point, we hypothesize that, firstly, the existence of a positive and strong association in the advanced stages of CKD is more evident, and secondly, the association between alcohol consumption and adverse outcomes can be influenced by the comorbid conditions, and it is necessary to consider patients' misbehaviors and comorbidities along with their alcohol consumption trend. For example, as mentioned earlier, individuals also tend to smoke while drinking alcohol, so the mentioned point can affect the adverse effects of alcohol consumption. In other words, smoking increases the oxidative stress damage of various organs due to alcohol consumption,[29] which worsens the kidney damage caused by alcohol abuse in patients with CKD.[19]

In addition, alcohol consumption can lead to increased volume overload, high blood pressure, and electrolyte imbalance between hemodialysis sessions in hemodialysis

Table 3: Evaluating the association between alcohol consumption and clinical and basic factors with the chronic kidney disease prevalence

Factors	Model 1		Model 2	
	OR (95 CI)	*P*	OR (95 CI)	*P*
Age >50 (year)			1.69 (0.52-0.93)	0.013
Sex, male			1.92 (1.46-2.52)	<0.001
BMI ≥25 (kg/m^2)			1.06 (0.83-1.36)	0.621
SBP			1.01 (0.99-1.01)	0.265
DBP			0.99 (0.98-1.01)	0.351
Creatinine			18.74 (3.54-59.20)	0.001
Microalbumin			1.03 (1.02-1.04)	<0.001
ACR			1.07 (1.06-1.08)	<0.001
FBG			0.99 (0.99-1.00)	0.271
LDL			0.99 (0.99-1.00)	0.153
HDL			0.98 (0.97-0.99)	0.037
Diabetes mellitus			1.29 (0.90-1.86)	0.160
Cerebrovascular disease			1.01 (0.69-1.46)	0.972
Musculoskeletal disease			0.95 (0.66-1.37)	0.775
Kidney stone			1.26 (0.95-1.67)	0.112
Hematuria			2.89 (1.75-4.76)	<0.001
Proteinuria			1.20 (0.54-2.67)	0.652
ARB			0.88 (0.63-1.22)	0.438
Beta-blocker			1.28 (0.71-2.31)	0.416
Antihyperlipidemic agents			0.82 (0.56-1.22)	0.328
Occasional drinking/nondrinking	1.32 (0.59-2.92)	0.499	1.21 (0.39-3.77)	0.739
Frequent drinking/nondrinking	0.54 (0.25-1.20)	0.132	0.58 (0.19-1.77)	0.339

Model 1=Nonadjusted; Model 2 was adjusted for age, sex, BMI, comorbidities (diabetes mellitus, cerebrovascular disease, musculoskeletal disease, kidney stone, hematuria, and proteinuria), clinical and laboratory parameters (SBP, DBP, creatinine, microalbumin, ACR, FBG, LDL, and HDL), and drugs (ARB, beta-blocker, and antihyperlipidemic agents). BMI=Body mass index; BP=Blood pressure; SBP=Systolic BP; DBP=Diastolic BP; ACR=Albumin-to-creatinine ratio; FBG=Fasting blood glucose; LDL=Low-density lipoprotein; HDL=High-density lipoprotein; ARB=Angiotensin receptor blockers; CI=Confidence interval; OR=Odds ratio

patients, which should not be ignored. Therefore, alcohol consumption can be considered a double-edged sword for patients with CKD, and any policy regarding their alcohol consumption should be applied very cautiously. However, in our study, its detrimental effect on the progression of high stages of CKD with and without adjusting the confounding factors was clearly evident. Perhaps, the strength of the present study was its attention to the confounding factors and patients' comorbidities along with the impact of alcohol consumption. In addition, the current study has examined the association between alcohol consumption trends and the odds of CKD prevalence, which has not been considered in any previous studies. However, given that patients' alcohol consumption data were recorded using the patients' self-statements that lack quantitative measurements, the mentioned point can be considered a limitation of this study as there may be the possibility of reporting lower amounts of alcohol consumption in patients' self-statements, and patients' alcohol consumption may be underestimated. Therefore, more clinical and experimental studies are required to confirm the effect of alcohol consumption on CKD. In addition, drinking trends, the correct dose of alcohol consumption, differences in alcoholic drinks, and various associated factors should also be considered as they appear to have a significant effect on the effects of alcohol consumption.

CONCLUSION

According to the results of the current study, alcohol consumption trends had a very weak and nonsignificant association with the odds of CKD prevalence and the odds of its progression from stage 2 CKD as compared with stage 1 CKD. However, adjusting the confounding factors indicated that occasional drinking as compared to nondrinking significantly increased the odds of stage 3 and 4 CKD prevalence as compared to stage 1 CKD prevalence. In addition to the association of alcohol consumption with different CKD stages, it was revealed that factors such as aging, history of cerebrovascular disease, and increased LDL and Cr can increase the odds of CKD prevalence at higher stages.

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Table 4: Evaluating the association between alcohol consumption and clinical and basic factors with different severity of chronic kidney disease

Factors	Model 1		Model 2	
	OR (95 CI)	*P*	OR (95 CI)	*P*
Stage 2 CKD versus Stage 1 CKD				
Age >50 years			6.74 (4.09-11.11)	<0.001
Sex, male			1.15 (0.67-1.96)	0.619
BMI ≥25 kg/m^2			0.86 (0.53-1.42)	0.561
SBP			1.01 (0.99-1.03)	0.384
DBP			0.99 (0.97-1.02)	0.832
Creatinine			0.90 (0.97-1.01)	0.710
Microalbumin			1.00 (0.99-1.03)	0.904
ACR			0.99 (0.99-1.01)	0.377
FBG			1.00 (0.99-1.01)	0.934
LDL			1.01 (1.00-1.02)	0.013
HDL			0.99 (0.97-1.01)	0.274
Diabetes mellitus			0.97 (0.49-1.91)	0.934
Cerebrovascular disease			3.24 (1.55-6.79)	0.002
Musculoskeletal disease			1.57 (0.71-3.46)	0.263
Kidney stone			0.75 (0.45-1.26)	0.283
Proteinuria			1.03 (0.30-3.52)	0.966
ARB			1.26 (0.66-2.42)	0.480
Beta-blocker			0.82 (0.29-2.31)	0.710
Antihyperlipidemic agents			0.94 (0.44-2.02)	0.873
Occasional drinking/nondrinking	0.93 (0.19-4.67)	0.821	0.96 (0.16-5.82)	0.962
Frequent drinking/nondrinking	0.47 (0.08-2.57)	0.871	0.41 (0.05-3.42)	0.413
Stage 2 and 3 CKD versus Stage 1 CKD				
Age >50 years			6.12 (4.41-40.79)	<0.001
Sex, male			1.10 (0.49-2.49)	0.816
BMI ≥25 kg/m^2			0.64 (0.27-1.49)	0.300
SBP			1.02 (0.99-1.05)	0.151
DBP			0.94 (0.89-0.98)	0.007
Creatinine			3.39 (1.55-10.36)	0.040
Microalbumin			0.99 (0.99-1.01)	0.157
ACR			1.00 (0.99-1.01)	0.633
FBG			0.99 (0.99-1.01)	0.394
LDL			1.01 (0.99-1.02)	0.603
HDL			0.95 (0.92-0.99)	0.018
Diabetes mellitus			1.02 (0.36-2.85)	0.972
Cerebrovascular disease			2.65 (0.92-7.64)	0.071
Musculoskeletal disease			2.76 (0.86-8.84)	0.087
Kidney stone			0.53 (0.22-1.27)	0.155
Proteinuria			1.37 (0.21-9.14)	0.742
ARB			1.46 (0.59-3.61)	0.410
Beta-blocker			0.59 (0.17-2.01)	0.402
Antihyperlipidemic agents			1.27 (0.44-3.68)	0.660
Occasional drinking/nondrinking	1.22 (0.20-7.37)	0.832	3.35 (1.47-17.09)	0.047
Frequent drinking/nondrinking	0.46 (0.05-4.12)	0.484	1.02 (0.06-8.72)	0.988

Model 1=Nonadjusted; Model 2 was adjusted for age, sex, BMI, comorbidities (diabetes mellitus, cerebrovascular disease, musculoskeletal disease, kidney stone, and proteinuria), clinical and laboratory parameters (SBP, DBP, creatinine, microalbumin, ACR, FBG, LDL, and HDL), and drugs (ARB, beta-blocker, and antihyperlipidemic agents). BMI=Body mass index; BP=Blood pressure; SBP=Systolic BP; DBP=Diastolic BP; ACR=Albumin-to-creatinine ratio; FBG=Fasting blood glucose; LDL=Low-density lipoprotein; HDL=High-density lipoprotein; ARB=Angiotensin receptor blockers; CKD=Chronic kidney disease; CI=Confidence interval; OR=Odds ratio

Conflicts of interest

There are no conflicts of interest.

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