Original Article

Coffee consumption is associated with lower serum aminotransferases in the general Korean population and in those at high risk for hepatic disease

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Background and Objectives: The favourable effects of coffee on liver enzymes have been reported worldwide. This study investigated the association between coffee consumption and serum aminotransferase concentration in Korean adults. **Methods and Study Design:** Data were obtained from the fourth and fifth Korea National Health and Nutrition Examination Surveys. Elevated alanine aminotransferase (ALT) and aspartate aminotransferase (AST) concentration were defined as >30 IU/L for men and >19 IU/L for women. The risk of elevated ALT and AST according to general characteristics and frequency of coffee consumption were tested by chi-square tests and multiple logistic regression analyses. **Results:** The prevalence of elevated ALT was 27.4%, 27.8%, and 26.9% in subjects who drank <1, 1, and ≥2 times/day, respectively. The proportions of individuals with elevated AST were 32.5%, 33.1%, and 26.7% in subjects who drank <1, 1, and ≥2 times/day, respectively. The aORs for elevated ALT and AST were significantly lower in subjects who drank ≥2 times of coffee/day than in those who drank <1 time/day (ALT: aOR=0.86, 95% CI=0.79-0.94; AST: aOR=0.83, 95% CI=0.76-0.91). In subgroup analysis, consumption of ≥2 times/day was associated with lower ORs for elevated ALT in the high-risk group overall and in the viral hepatitis and obesity subgroups, respectively. In sensitivity analysis, reduced frequency of coffee consumption was associated with an increased risk for elevated liver enzymes, although an association between coffee consumption and elevated ALT was not observed in women or current smokers. **Conclusions:** Higher coffee consumption was associated with lower risk of elevated aminotransferase concentration in Korean adults.

Key Words: adult, alanine transaminase, aspartate aminotransferases, coffee, risk factors

INTRODUCTION

Serum aminotransferase concentration are considered clinical indicators of liver health.[1] Chronic liver disease is often diagnosed by detecting asymptomatic high concentration of serum alanine aminotransferase (ALT) and aspartate aminotransferase (AST). Not all individuals with elevated aminotransferase activity have liver disease. However, some studies indicate that advanced liver disease, including cirrhosis, may be detected by slight increases in aminotransferase concentration.[2] Thus, measuring the prevalence of elevated aminotransferase activity in the general population may be a useful index of liver disease burden in a given population. In addition, the prevalence and predictors of elevated aminotransferase activity may also be important to guide recommendations for clinical evaluation of these laboratory abnormalities.[3]

The concentration of AST and ALT vary widely among populations, and the accuracy and applicability of previously established values for normal AST and ALT concentration is questionable.[4] The upper limits of normal ALT and AST concentration have been re-evaluated recently in various countries and suggest that the upper limit of normal should be revised to 30 U/L for men and 19 U/L for women.[5-7]

Recently, the favourable effects of coffee on liver enzymes have been reported worldwide.[8,9] According to data from the US National Health and Nutrition Examination Survey, consumption of coffee is associated with a lower risk of elevated ALT activity in individuals at high risk for liver injury.[10] Furthermore, elevated coffee consumption has been associated with reduced concentration of liver enzymes in patients co-infected with HIV and HCV.[11] Japanese studies also show that coffee consumption may have a beneficial effect on the stabilization of ALT concentration.[12,13]

Although coffee may have a favourable impact on liver disease, it has not been fully investigated in Korean popu-

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lations. A previously published study in Korea shows that heavy coffee drinkers (>20,000 cups over a lifetime) have significantly lower concentration of total cholesterol (TC), total protein, total albumin, and AST, although coffee consumption was not associated with ALT or gamma-glutamyl transpeptidase (GGT).[14] To the best of our knowledge, neither the prevalence of elevated liver enzymes according to the new cutoff values nor the beneficial effects of coffee consumption on liver enzymes has been investigated in the general Korean population. The purpose of this study was to investigate the association between coffee consumption and aminotransferase concentration in Korean adults.

MATERIALS AND METHODS

Data source

Data for this study were obtained from the fourth and fifth Korea National Health and Nutrition Examination Survey (KNHANES), cross-sectional examination surveys conducted by the Korean Centers for Disease Control and Prevention (KCDC) from 2007 to 2012. The KNHANES is based on a complex, multistage, probability sample design, and the study sample represents the total civilian noninstitutionalized population in Korea. This survey was comprised of three components: a health interview, a health examination, and a nutrition survey. The survey was approved by the institutional review board of the KCDC, and all participants provided written consent to participate.[15,16] The subjects in the present study were restricted to participants who reported coffee consumption frequency, and ALT and AST data were obtained from those who were at least 19 years of age (N =24,573).

Coffee consumption frequency

Coffee consumption was obtained using self-reported methods. Participants were asked how many times they drank coffee per day, per week, and per month. In the questionnaire, the frequency of coffee intake was classified into 10 categories: rarely, 6-11 times/year, 1 time/month, 2-3 times/month, 1 time/week, 2-3 times/week, 4-6 times/week, 1 time/day, 2 times/day, and ≥3 times/day. For this study, the frequency of coffee consumption was categorized into three groups (<1, 1, and ≥2 times/day, respectively). The KNHANES did not collect data on the type or the amount of coffee. No distinction was made between caffeinated versus decaffeinated coffee or between the individual types of coffee (boiled, filtered, and instant).[17]

Elevated aminotransferase concentration

In KNHANES, venous blood specimens were collected. Elevated ALT or AST concentration were defined as >30 IU/L for men and >19 IU/L for women. To compare our data with the data from previous studies, both the prevalence and odds ratios of serum AST >40 IU/L and ALT >40 IU/L were calculated.

Covariates

Independent variables included age group (19-44, 45-64, and 65+ years), sex (men vs women), education (less than high school, completed high school, and more than high school), household income, smoking status, drinking frequency, and physical activity.

High-risk group

The high-risk group included excessive alcohol intake, viral hepatitis, metabolic syndrome, diabetes mellitus, and obesity. Subgroups were not mutually exclusive.

- Excessive alcohol intake: excessive alcohol intake was defined as at least seven and five drinks per occasion for men and women, respectively.
- Viral hepatitis: HBV infection was defined as having both positive hepatitis B surface antigen serology and diagnosis by a doctor during a health interview. HCV infection was defined by a positive diagnosis by a doctor because KNHANES did not collect serology for HCV. We combined individuals infected with HBV and HCV into one category due to the very small numbers of individuals with either infection.
- Metabolic syndrome: metabolic syndrome was defined as having three or more of the following criteria: (1) abdominal obesity, defined as a waist circumference >90 cm for men and >80 cm for women; (2) triglycerides ≥150 mg/dL; (3) HDL cholesterol <40 mg/dL for men and <50 mg/dL for women; (4) blood pressure ≥130/85 mmHg or currently taking blood pressure medication; and (5) fasting glucose ≥100 mg/dL or currently taking medication for diabetes.
- Diabetes mellitus: diabetes was defined as having one of the following: (1) a medical history of diabetes, (2) currently taking medication for diabetes, or (3) a plasma glucose ≥126 mg/dL after ≥8-hour fast.
- Obesity: obesity was defined as a body mass index ≥25 kg/m^2.

Statistical analysis

General characteristics of the study subjects according to frequency of coffee consumption were analyzed using chi-square tests. The prevalence of elevated serum ALT or AST activity according to frequency of coffee consumption was also analyzed using chi-square tests. Odds ratios and 95% confidence intervals for elevated ALT or AST concentration according to coffee consumption frequency were calculated after controlling for other covariates. Additionally, trends of the odds ratios evaluating associations between elevated ALT or AST activity and coffee consumption frequency were coded as ordinal variables.

Additional analyses were conducted to examine the consistency of relationships between the frequency of coffee consumption and elevated ALT and AST activity within subgroups of individuals at high risk for liver injury. For sensitivity analyses, the association between coffee consumption frequency and elevated liver enzymes were evaluated by stratifying analyses according to sex, current smoking status, and alcohol consumption. All analyses incorporated sample weights, stratification, and clustering using SAS 9.2 software. A p-value <0.05 was considered statistically significant.

RESULTS

Subjects characteristics according to coffee consumption frequency

Approximately 36%, 24%, and 40% of subjects consumed <1 time/day, 1 time/day, and ≥2 times/day, respectively. Compared to individuals who consume <1 or 1 time/day, subjects who consumed ≥2 times of coffee/day were more likely to be younger, current smokers, and alcohol consumers at least twice per month (Table 1).

The prevalence of excessive alcohol intake, viral hepatitis, metabolic syndrome, diabetes mellitus, and obesity were 11.1%, 3.9%, 22.2%, 9.2%, and 29.4%, respectively. The prevalence of excessive alcohol intake, viral hepatitis, and obesity was higher in subjects who drank ≥2 times of coffee per day (Table 1).

Prevalence of elevated aminotransferase concentration according to coffee consumption frequency

Prevalence of elevated ALT, when defined as >30 IU/L in men and >19 IU/L in women, was 27.3% overall, 15.9% in the low-risk group, and 38.5% in the high-risk groups. The prevalence of elevated AST according to the above definitions was 30.3% overall, 24.2% in the low-risk

Table 1. Characteristics of study subjects according to coffee consumption frequency

Characteristics	Coffee (times/day)			*p*-value
	<1	1	≥2	
Total	8,887 (36.3)	6,226 (23.9)	9,460 (39.8)	
Sex				<0.001
Men	3,106 (42.2)	2,123 (39.1)	4,680 (55.2)	
Women	5,781 (57.8)	4,103 (60.9)	4,780 (44.8)	
Age (years)				<0.001
19-44	3,596 (54.8)	2,297 (47.6)	4,286 (52.4)	
45-64	2,786 (28.5)	2,358 (36.1)	3,735 (38.9)	
≥65	2,505 (16.7)	1,571 (16.3)	1,439 (8.8)	
Mean±SE	43.7±0.31	46.8±0.31	45.1±0.21	
Education				<0.001
≤Elementary school	2,972 (23.3)	1,875 (22.8)	1,885 (15.2)	
Middle school	884 (8.7)	775 (11.9)	1,131 (11.6)	
≥High school	4,975 (68.0)	3,550 (65.3)	6,385 (73.2)	
Household income				<0.001
Low	2,200 (19.5)	1,318 (17.7)	1,410 (12.2)	
Middle-low	2,200 (26.1)	1,549 (25.6)	2,351 (26.2)	
Middle-high	2,205 (28.4)	1,605 (27.8)	2,790 (31.1)	
High	2,086 (26.0)	1,663 (28.9)	2,771 (30.5)	
Smoking status				<0.001
Never	6,029 (63.3)	4,068 (60.8)	4,699 (44.9)	
Former	1,641 (19.0)	1,209 (19.9)	1,975 (20.9)	
Current	1,173 (17.7)	935 (19.2)	2,739 (34.2)	
Drinking frequency				<0.001
None	3,273 (29.7)	1,861 (26.3)	1,946 (17.3)	
≤Once/month	2,515 (29.8)	1,951 (31.2)	2,753 (29.0)	
≥Twice/month	3,033 (40.5)	2,374 (42.5)	4,680 (53.6)	
Physical activity				0.125
No	6,913 (77.1)	4,782 (77.4)	7,167 (75.8)	
Yes	1,974 (22.9)	1,444 (22.6)	2,293 (24.2)	
Low-risk group	4,426 (52.2)	2,987 (49.5)	4,527 (47.1)	<0.001
High-risk group†	4,461 (47.8)	3,239 (50.5)	4,933 (52.9)	
Excessive alcohol intake	789 (11.1)	564 (10.8)	1,172 (14.9)	<0.001
Viral hepatitis	371 (3.9)	75 (4.3)	502 (5.7)	<0.001
Metabolic syndrome	2,417 (22.2)	1,767 (25.3)	2,175 (21.2)	<0.001
Diabetes mellitus	1,033 (9.2)	692 (9.7)	788 (7.3)	<0.001
Obesity	2,616 (29.4)	1,965 (30.6)	3,170 (34.5)	<0.001

Data are expressed as the number (weighted %). SE: standard error.

†The high-risk group included excessive alcohol intake, viral hepatitis, metabolic syndrome, diabetes mellitus, and obesity. Subgroups are not mutually exclusive.

- Excessive alcohol intake is defined as at least seven and five drinks per occasion for men and women, respectively.
- Viral hepatitis is defined as history of hepatitis B and/or C infection or HBsAg-positive status.
- Metabolic syndrome is defined as increased waist circumference (≥90 cm for men and ≥80 cm for women), high triglyceride concentration (≥15 mg/dL), low high-density lipoprotein concentration (<40 mg/dL for men and <50 mg/dL for women), elevated blood pressure (systolic blood pressure ≥130 mmHg, diastolic blood pressure ≥85 mmHg, or antihypertensive medication), and elevated glucose concentration (fasting blood glucose ≥100 mg/dL, hypoglycemic medication, or insulin use).
- Diabetes mellitus is defined as a previous diagnosis of diabetes or fasting blood glucose ≥126 mg/dL, hypoglycemic medication, or insulin use.
- Obesity is defined as a body mass index greater than or equal to 25 kg/m^2.

Table 2. Proportion of elevated liver enzymes according to coffee consumption frequency

	Total	Coffee (times/day)			*p*-value
		<1	1	≥2	
Elevated ALT†					
Entire subjects	27.3 (0.5)	27.4 (0.7)	27.8 (0.8)	26.9 (0.6)	0.590
Low-risk group	15.9 (0.5)	16.1 (0.8)	17.1 (1.0)	14.8 (0.7)	0.130
High-risk group	38.5 (0.6)	39.8 (1.1)	38.3 (1.1)	37.6 (0.8)	0.234
Excessive alcohol intake	29.1 (1.1)	30.1 (2.1)	28.0 (2.4)	28.9 (1.6)	0.795
Viral hepatitis	42.2 (1.8)	47.8 (3.1)	45.3 (4.0)	37.3 (2.5)	0.028
Metabolic syndrome	47.4 (0.8)	48.5 (1.5)	44.6 (1.5)	48.4 (1.3)	0.113
Diabetes mellitus	43.6 (1.2)	42.8 (2.1)	41.8 (2.3)	46.1 (2.3)	0.385
Obesity	44.4 (0.8)	46.4 (1.5)	43.5 (1.4)	43.4 (1.1)	0.180
Elevated AST‡					
Entire subjects	30.3 (0.5)	32.5 (0.8)	33.1 (0.8)	26.7 (0.6)	<0.001
Low-risk group	24.2 (0.6)	25.4 (0.9)	26.9 (1.1)	21.2 (0.8)	<0.001
High-risk group	36.4 (0.6)	40.3 (1.1)	39.1 (1.1)	31.7 (0.9)	<0.001
Excessive alcohol intake	26.5 (1.1)	29.2 (2.1)	27.1 (2.1)	24.4 (1.5)	0.128
Viral hepatitis	45.9 (1.9)	53.6 (3.2)	46.9 (3.7)	40.6 (2.8)	0.007
Metabolic syndrome	45.6 (0.9)	50.7 (1.4)	46.7 (1.5)	39.8 (1.4)	<0.001
Diabetes mellitus	39.8 (1.3)	44.9 (2.1)	39.0 (2.3)	34.5 (2.2)	0.002
Obesity	37.6 (0.8)	40.9 (1.4)	41.4 (1.5)	33.1 (1.0)	<0.001

ALT: alanine aminotransferase; AST: aspartate aminotransferase
Data are expressed as the weighted % (standard error).
†Elevated ALT is defined as ALT >30 IU/L for men and >19 IU/L for women.
‡Elevated AST is defined as AST >30 IU/L for men and >19 IU/L for women.

group, and 36.4% in the high-risk groups (Table 2).

Among subgroups at high risk for liver injury, the prevalence of elevated ALT activity was 29.1% in the excessive alcohol intake, 42.2% in the viral hepatitis, 47.4% in the metabolic syndrome, 43.6% in the diabetes mellitus, and 44.4% in the obesity subgroup. The prevalence of elevated AST activity was 26.5% in the excessive alcohol intake, 45.9% in the viral hepatitis, 45.6% in the metabolic syndrome, 39.8% in the diabetes mellitus, and 37.6% in the obesity subgroup (Table 2).

The proportion of elevated ALT concentration did not significantly differ according to coffee consumption frequency. The proportion of elevated AST concentration significantly differed according to coffee consumption frequency in both the low- and high-risk groups (Table 2).

Odds ratios for elevated aminotransferase by coffee consumption frequency

After controlling for sex, age, smoking status, and body mass index, subjects who drank at least 2 times per day had significantly lower risk for elevated ALT or AST activity than those who drank <1 time per day (ALT: odds ratio=0.86, 95% confidence interval=0.79-0.94; AST: odds ratio=0.83; 95% confidence interval=0.76-0.91). In subgroup analysis, higher frequency of coffee consumption was associated with a lower risk for elevated ALT concentration in groups with viral hepatitis and obesity (Table 3).

Results from sensitivity analyses are summarized in Table 4. Stratification by sex and current smoking and drinking status showed similar results. Reduced frequency of coffee consumption was associated with an increased risk for elevated liver enzymes, although an association between coffee consumption and elevated ALT was not observed in women or current smokers.

DISCUSSION

This study examined the prevalence of elevated aminotransferase activity and its association with coffee consumption in a representative sample of Korean adults. Our findings indicated that the odds of elevated aminotransferase concentration were significantly lower in subjects who consumed coffee more frequently.

The overall prevalence of elevated ALT and AST were 27.3 and 30.3%, respectively. In the low-risk group (i.e., patients that did not have known risk factors for elevated aminotransferase concentration), the prevalence of elevated ALT and AST was 15.9% and 24.2%, respectively. These were substantially higher than those from Korean populations in previous publications.[18,19] Using the conventional cutoff values for both ALT and AST (>40 IU/L for both men and women), the prevalence of elevated aminotransferase concentration decreased to 8.8% for ALT and 4.6% for AST. Stratifying the data according to the risk for liver disease showed that the prevalence of elevated ALT was 3.4% and 14.0% in the low- and high-risk groups, respectively. Similarly, the prevalence of elevated AST concentration was 1.8% and 7.4% in the low- and high-risk groups, respectively. These differences in prevalence are primarily due to the different cutoff values for elevated aminotransferase concentration and the different definitions for the high-risk groups. Thus, both cutoff values and definition of high-risk groups should be considered when defining elevated aminotransferase activity.

We suspect that most cases of unexplained elevations in aminotransferase concentration were caused by non-alcoholic fatty liver disease (NAFLD) in our study. Previous studies show that NAFLD is the most common cause of elevated aminotransferase concentration in the absence of viral hepatitis or excessive alcohol consumption.[3,20] However, we could not determine the true cause of elevated aminotransferase concentration for individuals

Table 3. Odds ratios for elevated liver enzymes according to coffee consumption frequency

	Coffee (times/day)			*p* for trend
	<1	1	≥2	
Elevated ALT†				
Entire subjects	1.00	0.95 (0.86-1.05)	0.86 (0.79-0.94)	0.001
Low-risk group	1.00	1.00 (0.84-1.19)	0.84 (0.72-0.98)	0.030
High-risk group	1.00	0.92 (0.81-1.04)	0.88 (0.78-0.98)	0.023
Excessive alcohol intake	1.00	0.87 (0.63-1.20)	0.83 (0.64-1.08)	0.163
Viral hepatitis	1.00	0.87 (0.56-1.37)	0.66 (0.48-0.92)	0.123
Metabolic syndrome	1.00	0.85 (0.72-1.01)	0.90 (0.77-1.06)	0.218
Diabetes mellitus	1.00	0.98 (0.74-1.30)	1.21 (0.91-1.60)	0.206
Obesity	1.00	0.89 (0.75-1.04)	0.86 (0.74-0.99)	0.041
Elevated AST‡				
Entire subjects	1.00	0.92 (0.83-1.01)	0.83 (0.76-0.91)	<0.001
Low-risk group	1.00	0.93 (0.81-1.08)	0.80 (0.70-0.92)	0.002
High-risk group	1.00	0.90 (0.80-1.02)	0.86 (0.76-0.96)	0.009
Excessive alcohol intake	1.00	0.88 (0.65-1.20)	0.80 (0.62-1.04)	0.091
Viral hepatitis	1.00	0.66 (0.42-1.06)	0.78 (0.51-1.18)	0.282
Metabolic syndrome	1.00	0.88 (0.74-1.06)	0.88 (0.73-1.05)	0.138
Diabetes mellitus	1.00	0.86 (0.65-1.13)	0.90 (0.67-1.21)	0.442
Obesity	1.00	0.98 (0.83-1.15)	0.88 (0.76-1.02)	0.078

ALT: alanine aminotransferase; AST: aspartate aminotransferase
Data are expressed as the adjusted odds ratio (95% confidence interval). Odds ratios were calculated after adjusting for sex, age, smoking status, and body mass index.
†Elevated ALT is defined as ALT >30 IU/L for men and >19 IU/L for women.
‡Elevated AST is defined as AST >30 IU/L for men and >19 IU/L for women.

Table 4. Association between coffee consumption frequency and elevated liver enzymes in subgroups according to sex, smoking status, and drinking status

	Coffee (times/day)			*p*-value
	<1	1	≥2	
Elevated ALT†				
Sex‡				
Men	1.00	0.88 (0.74-1.05)	0.85 (0.74-0.98)	0.031
Women	1.00	0.99 (0.87-1.12)	0.91 (0.81-1.03)	0.138
Current smoking§				
No	1.00	0.97 (0.88-1.08)	0.87 (0.79-0.97)	0.008
Yes	1.00	0.79 (0.59-1.05)	0.85 (0.68-1.05)	0.180
Current drinking¶				
No	1.00	0.79 (0.66-0.95)	0.92 (0.77-1.10)	0.226
Yes	1.00	1.02 (0.90-1.15)	0.87 (0.78-0.97)	0.009
Elevated AST††				
Sex‡				
Men	1.00	0.82 (0.67-0.99)	0.78 (0.66-0.93)	0.005
Women	1.00	0.95 (0.85-1.06)	0.87 (0.79-0.98)	0.016
Current smoking§				
No	1.00	0.93 (0.84-1.03)	0.82 (0.75-0.91)	<0.001
Yes	1.00	0.77 (0.59-0.99)	0.82 (0.66-1.02)	0.110
Current drinking¶				
No	1.00	0.80 (0.68-0.93)	0.84 (0.70-0.99)	0.022
Yes	1.00	0.97 (0.87-1.08)	0.84 (0.76-0.94)	0.001

ALT: alanine aminotransferase; AST: aspartate aminotransferase
Data are expressed as the adjusted odds ratio (95% confidence interval).
†Elevated ALT is defined as ALT >30 IU/L for men and >19 IU/L for women.
‡Odds ratios were calculated after adjusting for age, smoking status, drinking status, and body mass index.
§Odds ratios were calculated after adjusting for sex, age, drinking status, and body mass index.
¶Odds ratios were calculated after adjusting for sex, age, smoking status, and body mass index.
††Elevated AST is defined as AST >30 IU/L for men and >19 IU/L for women.

in our study because KNHANES did not collect tissue samples for histology. NAFLD is strongly associated with many predictors of cardiovascular disease[21] and is regarded as a major cause of cirrhosis and hepatocellular carcinoma.[22,23]

This study showed a significant association between elevated coffee consumption and reduced liver enzyme concentration in the general Korean population. Furthermore, the protective role of coffee was observed regardless of the risk factor for liver injury (i.e., excessive alcohol intake, viral hepatitis, abnormal glucose status, or obesity) and was consistent with previous international

literature demonstrating the protective effects of coffee on the liver.[10,11,13] According to a U.S. study of the NHANES database, consumption of coffee is associated with a lower risk for abnormal ALT activity in individuals at high risk for liver injury, as individuals who report drinking >2 cups per day have approximately one-half the risk of non-coffee drinkers.[10] Two recent meta-analyses also suggest an inverse relationship between coffee drinking and the risk of hepatocellular carcinoma.[24,25]

Several potential mechanisms may explain the role of coffee consumption in reducing the risk of elevated aminotransferase activity. Coffee contains a variety of chemicals, including caffeine, cafestol, kahweol, and chlorogenic acids, although the coffee ingredients that have liver-protective properties are unclear. Polyphenols have significant anti-inflammatory activity,[26] and antioxidants have been found in aroma extracts isolated from coffee beans. According to animal studies, diterpenes (non-triglyceride lipid components of coffee oils), cafestol, and kahweol induce the synthesis of glutathione, an important mediator against hepatocellular injury.[27] These studies suggest that ingredients in coffee may play a protective role in the liver.

In this study, we conducted subgroup analyses according to known risk factors for liver injury. The association between coffee and the aminotransferase concentration was quite different among the disease subgroups. Pathophysiological processes associated with such conditions may have diminished the modest serum aminotransferase-lowering effects of coffee. Furthermore, subjects who have these conditions may have changed their lifestyles following the diagnosis.[12] Therefore, the inclusion and exclusion criteria for study population and subgroup analyses are important for investigating the association between coffee and liver health.

The current study had several limitations. We could not establish a temporal association between coffee and caffeine consumption and abnormal ALT activity due to the cross-sectional nature of KNHANES. Additionally, information on the type of coffee, brewing method, and degree of roasting was not available from the survey. Growth conditions, including the type of coffee plant (usually Robusta and Arabica), sorting procedures, removal of flesh, fermentation, and washing and drying of the beans, as well as the roasting and brewing processes affect the quality, composition, and biological capabilities of coffee.[13,28] Thus, further studies are needed to investigate the effects of coffee consumption on the aminotransferase concentration according to the type and amount of coffee in each beverage.

In summary, the prevalence of elevated ALT and AST concentration (>30 IU/L for men and >19 IU/L for women) was 27.3% and 30.3% overall, 15.9% and 24.2% in the low-risk group, and 38.5% and 24.2% in the high-risk groups, respectively. Consumption of ≥2 times of coffee per day was significantly associated with a lower risk of elevated aminotransferase concentration, although an association between coffee consumption and elevated ALT was not observed in women or current smokers. Our results indicating that regular coffee consumption may be beneficial for preventing elevated aminotransferase concentration in subjects with or without the known risk factors for liver injury.

AUTHOR DISCLOSURES

The authors have no potential conflicts of interest to declare.

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Supplementary table 1. Proportion of individuals with elevated liver enzymes according to coffee consumption frequency

	Total	Coffee (times/day)			*p*-value
		<1	1	≥2	
Elevated ALT†					
Entire subjects	8.8 (0.2)	8.5 (0.4)	7.4 (0.4)	9.8 (0.4)	<0.001
Low-risk group	3.4 (0.2)	3.6 (0.4)	3.0 (0.4)	3.5 (0.4)	0.560
High-risk group	14.0 (0.4)	13.8 (0.7)	11.8 (0.8)	15.5 (0.6)	0.002
Excessive alcohol intake	14.6 (0.8)	14.7 (1.5)	13.1 (1.6)	15.2 (1.3)	0.638
Viral hepatitis	14.8 (1.3)	18.8 (2.7)	9.2 (2.2)	14.7 (1.9)	0.033
Metabolic syndrome	17.2 (0.6)	14.4 (1.0)	14.7 (1.1)	21.7 (1.2)	<0.001
Diabetes mellitus	17.2 (1.0)	14.4 (1.7)	15.9 (1.7)	21.4 (1.9)	0.010
Obesity	17.1 (0.6)	16.7 (1.0)	14.8 (1.1)	18.6 (0.9)	0.028
Elevated AST‡					
Entire subjects	4.6 (0.2)	5.1 (0.3)	3.8 (0.3)	4.6 (0.3)	0.017
Low-risk group	1.8 (0.2)	2.1 (0.3)	1.6 (0.3)	1.7 (0.3)	0.410
High-risk group	7.4 (0.3)	8.2 (0.6)	6.1 (0.5)	7.2 (0.5)	0.010
Excessive alcohol intake	10.3 (0.8)	11.5 (1.3)	9.1 (1.3)	10.0 (1.2)	0.486
Viral hepatitis	12.2 (1.4)	17.4 (2.8)	8.3 (2.2)	10.8 (2.0)	0.022
Metabolic syndrome	9.0 (0.5)	9.4 (0.9)	7.9 (0.8)	9.4 (0.8)	0.383
Diabetes mellitus	11.3 (0.9)	10.8 (1.3)	9.7 (1.3)	13.0 (1.6)	0.243
Obesity	7.5 (0.4)	8.1 (0.8)	6.9 (0.7)	7.3 (0.6)	0.460

ALT: alanine aminotransferase; AST: aspartate aminotransferase
Data are expressed as the weighted % (standard error).
†Elevated ALT is defined as ALT >40 IU/L.
‡Elevated AST is defined as AST >40 IU/L.

Supplementary table 2. Odds ratios for elevated liver enzymes according to coffee consumption frequency

	Coffee (times/day)			*p* for trend
	<1	1	≥2	
Elevated ALT†				
Entire subjects	1.00	0.85 (0.71-1.01)	0.87 (0.75-1.02)	0.106
Low-risk group	1.00	0.85 (0.58-1.24)	0.82 (0.59-1.13)	0.225
High-risk group	1.00	0.84 (0.69-1.03)	0.88 (0.75-1.04)	0.172
Excessive alcohol intake	1.00	0.84 (0.56-1.29)	0.87 (0.63-1.22)	0.448
Viral hepatitis	1.00	0.34 (0.18-0.65)	0.55 (0.33-0.90)	0.040
Metabolic syndrome	1.00	1.04 (0.80-1.36)	1.04 (0.82-1.32)	0.759
Diabetes mellitus	1.00	1.12 (0.74-1.68)	1.11 (0.76-1.62)	0.605
Obesity	1.00	0.91 (0.72-1.15)	0.93 (0.76-1.14)	0.500
Elevated AST‡				
Entire subjects	1.00	0.68 (0.55-0.85)	0.67 (0.55-0.82)	<0.001
Low-risk group	1.00	0.79 (0.50-1.23)	0.69 (0.43-1.11)	0.125
High-risk group	1.00	0.66 (0.52-0.84)	0.67 (0.53-0.83)	0.001
Excessive alcohol intake	1.00	0.73 (0.48-1.13)	0.76 (0.52-1.11)	0.180
Viral hepatitis	1.00	0.36 (0.19-0.71)	0.49 (0.28-0.85)	0.021
Metabolic syndrome	1.00	0.79 (0.57-1.09)	0.67 (0.49-0.93)	0.017
Diabetes mellitus	1.00	0.83 (0.56-1.24)	0.84 (0.56-1.26)	0.403
Obesity	1.00	0.80 (0.59-1.10)	0.74 (0.55-0.98)	0.041

ALT: alanine aminotransferase; AST: aspartate aminotransferase
Data are expressed as the adjusted odds ratio (95% confidence interval). Odds ratios were calculated after adjusting for sex, age, smoking status, and body mass index.
†Elevated ALT is defined as ALT >40 IU/L.
‡Elevated AST is defined as AST >40 IU/L.

Original Article

Coffee consumption is associated with lower serum aminotransferases in the general Korean population and in those at high risk for hepatic disease

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韩国一般人群和肝病高风险人群咖啡消费量与较低的血清转氨酶有关

背景和目的：咖啡对肝酶的有利影响已在世界范围内被报道。该研究调查了在韩国成年人的咖啡消费量和血清转氨酶浓度之间的关系。**方法与研究设计：**数据来自第四和第五次韩国国家健康和营养检测普查。男性丙氨酸氨基转移酶（ALT）和谷草转氨酶（AST）大于 30 IU/L，女性大于 19 IU/L 为升高。采用卡方检验和多因素 Logistic 回归分析，探讨一般特征和咖啡消费频率与 ALT 和 AST 升高的风险。**结果：**咖啡摄入频率<1，1 和≥2 次/天的人群高 ALT 的发生率分别为 27.4%、27.8%和 26.9%，高 AST 的发生率分别为 32.5%、33.1%和 26.7%。咖啡摄入频率≥2 次/天的人群比<1 次/的人群调整 OR 显著降低（ALT：aOR=0.86，95% CI =0.79-0.94；AST：aOR=0.83，95% CI=0.76-0.91）。亚组分析显示，高危人群整体以及病毒性肝炎组和肥胖组中咖啡摄入频率≥2 次/天的人群 ALT 升高的风险低。敏感性分析显示：减少咖啡消费频率与肝酶升高的风险增加相关，但在女性和当前吸烟者中并未发现咖啡消费量与 ALT 升高之间的关系。**结论：**韩国成人较高的咖啡消费量与氨基转移酶浓度升高的风险较低有关。

关键词：成人、丙氨酸转氨酶、天冬氨酸转氨酶、咖啡、危险因素