Different associations of specific non-alcoholic beverages with elevated high-sensitivity C-reactive protein in Korean adults: results from the Korea National Health and Nutrition Examination Survey (2015–2016)

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This study examined the associations between specific non-alcoholic beverages and high-sensitivity C-reactive protein (hs-CRP) and their interactions with obesity. The study participants were 4,999 adults aged 19–64 years from the 2015–2016 Korean National Health and Nutrition Examination Survey. The odds ratios (ORs) and 95% confidence intervals (CIs) were obtained using multivariable logistic regression analyses. In women, there was an inverse linear trend between coffee and hs-CRP status ($p_{trend} = 0.0137$), and a positive linear trend for soda was also found (≥1/week vs never or almost never, OR = 1.79, 95% CI 1.23–2.61, $p_{trend} = 0.0127$). In the stratification analyses, the associations were only observed in obese women. The associations were inverse for coffee and tea but linearly positive for soda in obese women ($p_{trend}<0.05$). In men, an inverted J-shaped association between commercial fruit juice/drink and hs-CRP status was found; but after stratification by obesity, the association was linear only in obese men ($p_{trend}<0.05$, OR = 2.44, 95% CI 1.44–4.16 in ≥1/week vs never or almost never). Coffee and tea in women may be beneficially associated with hs-CRP status, but soda in women and commercial fruit juice/drink in men may be adversely, particularly for obese adults.

***Key Words*: coffee, green tea, soda, fruit juice, hs-CRP, inflammation**

High-sensitivity C-reactive protein (hs-CRP), which is a chronic and systemic low-grade inflammation marker, is associated with the development of lifestyle-related chronic diseases such as cardiovascular disease (CVD).[1] Nevertheless, there is little evidence on the determinants of hs-CRP level including dietary factors, although consumption of fruits and vegetables rich in antioxidants and anti-inflammatory nutrients has been known to be inversely associated with hs-CRP level.[2,3]

Recently, sugar-sweetened beverages (SSBs) such as soft drinks, which belongs to non-alcoholic beverages (NABs), have become an important public health concern worldwide due to their excess calories.[4–8] They have been intensively studied and a meta-analysis reported a clear positive association between increased energy intake from soft drinks and body weight.[6,7,9] In addition, NABs were previously studied on the association with hs-CRP,[10–12] but results for specific-NABs such as fruit drinks, tea, and coffee[10–12] were not consistent. It may be because many components, besides the content of sugar or sweeteners, varies, depending on the type of beverages; for example, caffeine, polyphenols, and minerals[13,14] in coffee and flavonoids, catechins, and caffeine in green tea[15] may be beneficial for inflammation, but sugar or high fructose corn syrup (HFCS) in soda[8] and high fructose content in commercial fruit juice/drinks[16] may be harmful.

A recent report from the US National Health and Nutrition Examination Survey (NHANES) demonstrated the altered association of SSBs with CRP level by obesity status.[17] Obesity has become a major public health concern worldwide, because it is a well-established risk factor for chronic diseases such as CVD, diabetes, and some cancers. Thus, an enhanced understanding of the relationship of beverage consumption with hs-CRP level regarding obesity status may contribute to the development of strategies to prevent inflammatory chronic diseases.

Therefore, we investigated the associations of specific NABs (total coffee, sugar-sweetened, non-sugar sweetened coffee, green tea, commercial fruit juice/drink, and soda) with hs-CRP status among Korean adults from the 2015–2016 Korean National Health and Nutrition Examination Survey (KNHANES) and additionally examined whether the association between NABs and hs-CRP status was modified by obesity status.

Methods

Study population. The KNHANES is conducted by the Ministry of Health and Welfare and the Korea Centers for Disease Control and Prevention (KCDC). We used the KNHANES data collected in 2015 and 2016. Participants were selected from the stratified multistage probability samples of Korean households. Data were collected in accordance with a standardized protocol by trained investigators. Detailed information about the KNHANES is available elsewhere[18] and has been described on the website (https://knhanes.cdc.go.kr/).

A total of 6,672 participants completed the food frequency questionnaire (FFQ) among adults aged 19–64 years ($n = 9{,}147$). We excluded pregnant or lactating women ($n = 138$), who had any cancer ($n = 203$) or CVD ($n = 103$) diagnosed by physicians, who had implausible energy intake (≥99.5th or ≤0.5th percentile of total energy intake by sex, $n = 64$), who had diabetes ($n =$

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244), who did not have hs-CRP levels available ($n = 408$) or hs-CRP levels over 10 mg/L ($n = 75$),[19] or fasted less than 8 h before blood testing ($n = 124$). After additionally excluding missing data for covariates such as house income, education status, and alcohol consumption status ($n = 314$), total 4,999 participants (1,984 men and 3,015 women) remained for inclusion in the analyses. The KNHANES was conducted by the Korean government under the Bioethics and Safety Act and the Enforcement Rule within the Act and thus the present study was exempt from approval by an Institutional Review Board.

Assessment of non-alcoholic beverages (NABs) consumption. Dietary data were collected by face-to-face interview at home using a 112-items semi-quantitative FFQ which was developed and validated by KCDC.[20] Participants were asked to specify their usual frequency and the average portion size of each food during the previous year. In the FFQ, five NABs were assessed: coffee, green tea, commercial fruit juice/drink (excluding homemade fruit juice), soda, and a traditional grain-based beverage including Sikhye and Misugaru. However, the traditional grain-based beverage was not used in the present study, because we could not characterize these items including several kinds of beverages as one common property. We calculated how many servings were consumed per month, week, or day for each NAB by multiplying the usual frequency of consumption by its portion size. We classified participants into three groups for four NABs (Never or almost never, ≥1/month to <1/day, and ≥1/day for total coffee; Never or almost never, ≥1/month to <1/week, and ≥1/week for green tea, commercial fruit juice, and soda). For coffee, participants were asked to respond to the additional questions about the frequency and amount of sugar added to coffee. Participants were classified into four groups; non-coffee drinkers, only sugar-sweetened coffee drinkers (SS-coffee), only non-sugar sweetened coffee drinkers (NSS-coffee), and both types of coffee drinkers.

Assessment of covariates: demographics and lifestyle. Sociodemographic, general health status, medical history, and health-related behaviors were obtained by face-to-face interviews. Family income was classified into 'lower middle or less' and 'upper middle or over'. Education was classified into 'college or more' and 'less than college'. Current drinker was defined as a person who consumed alcohol more than once per month during the previous year. Physically active person was defined as a person who performed moderate-intensity activities for ≥150 min/week or vigorous-intensity activities for ≥75 min/week based on the World Health Organization (WHO) physical activity guidelines.[21] To quantify adherence to dietary guidelines for Korean adults, the Korean Healthy Eating Index (KHEI) was calculated using FFQ data.[22] However, the empty calorie food items, a component of the KHEI including SSBs and added sugar to coffee, were excluded from the KHEI calculation.

Assessment of obesity status. Height to the nearest 0.1 cm was measured using a portable stadiometer. Weight to the nearest 0.1 kg was measured using a portable electronic scale. Body mass index (BMI) was calculated as weight (kg)/height (m^2). Waist circumference (WC) was measured to the nearest 0.1 cm at the midpoint between the bottom of the rib cage and above the top of the iliac crest. Obesity was defined as BMI ≥25 kg/m^2 in accordance with the Asia-Pacific criteria of the WHO guidelines.[23] Abdominal obesity was defined as WC ≥90 cm for men and ≥85 cm for women, in accordance with the definition of the Korean Society for the Study of Obesity.[24]

Assessment of high-sensitivity C-reactive protein (hs-CRP). Serum hs-CRP levels were measured using immunoturbidimetry with a range from 0.1 to 20.0 mg/L with a Roche Cardiac C-Reactive Protein High Sensitive detector (Roche, Penzberg, Germany). After excluding participants with hs-CRP over 10 mg/L, we classified participants into elevated hs-CRP level (≥2.0 mg/L) and normal hs-CRP level (<2.0 ml/L) according to the cutoff recommended by the American College of Cardiology and American Heart Association (ACC/AHA) Task Force on the assessment of cardiovascular risk.[1]

Statistical analysis. All analyses were stratified by sex. To account for the complex sampling design, the primary sampling units, strata, clusters, and weights were applied to all analyses (PROC SURVEY) to represent the Korean population. Data are presented as means ± SE for continuous variables and the number of participants (weighted percentages) for categorical variables. Covariates between groups of each NAB were compared by Rao-Scott chi-square tests for categorical variables and by the general linear model (GLM) analyses for continuous variables. The differences in mean values between each NAB groups were assessed by Tukey's multiple comparison test. The linear trend was obtained by treating the median value for the specific-NAB group as a continuous value. Multivariable logistic regression analyses were performed to obtain adjusted odds ratios (ORs) and 95% confidence intervals (CIs) for elevated hs-CRP status by NAB consumption.

Factors associated with hs-CRP in the previous studies were considered as potential confounders: age, adiposity status,[25] socioeconomic status,[26] cigarette smoking,[27] alcohol consumption,[28] physical activity,[29] menopausal status, dietary intake,[22,30] and consumption of 6 different types of NABs in servings/week.[31] Among those variables, variables showing significant statistical difference (p_{diff}) or linear trend (p_{trend}), but not highly correlated with individual NABs (the partial correlation with age, $r \geq 0.60$), were selected as confounders to obtain a more parsimonious model. In the analysis of sugar-containing beverages (e.g., SS-coffee, fruit juice/drink, soda), we did not include BMI and WC as confounders because of their possible roles as mediators.[10,32] Additionally, the stratified analyses by obesity (BMI ≥25 kg/m^2 vs <25 kg/m^2, WC ≥90 cm vs <90 cm for men and ≥85 cm vs <85 cm for women) were conducted. The interaction analyses of NABs with obesity status were conducted in the logistic regression at significance $p<0.05$. The associations between types of coffee and hs-CRP status were analyzed using non-coffee drinkers as a reference group. To visualize dietary patterns in relation to each NAB, the percentage-wise differences in median consumption of nineteen food groups in the lowest and highest consumptions of specific beverage relative to the median consumption of total population (equivalent to 100%) were illustrated in radar charts (Supplemental Fig. 1*).[33]

All statistical tests were performed by using SAS statistical software (ver. 9.4; SAS Institute Inc., Cary, NC) or statistical R software ver. 4.0.0. for the radar chart. A two-tailed p value <0.05 was considered statistically significant.

Results

The proportion of men was 39.7%, and the mean age was 39.4 years for men and 41.1 years for women. Men were more likely to be highly educated, smokers, and consumers of alcohol than women and also to have higher intakes of energy, SS-coffee, green tea, fruit juice/drink, and soda and higher BMI. However, for HEI and NSS-coffee, women were more likely to be higher (Table 1).

Table 2 shows that higher coffee consumers tended to be older, higher educated, smokers, and consumers of alcohol and to have higher BMIs and WCs. Higher coffee consumers also had higher energy intake but lower HEI. There were some differences in characteristics according to other NABs (Supplemental Table 1–4*). Table 3 presents the associations of NAB consumption with hs-CRP status by sex after adjusting for confounders selected from Table 2 and Supplemental Table 1–4* and demonstrates the association of NABs with hs-CRP status in non-obese and obese groups. In women, there was an inverse association between total coffee consumption and hs-CRP status ($p_{trend} = 0.014$) but a

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Table 1. Weighted characteristics of participants (n = 4,999)

Variables	Men (n = 1,984)	Women (n = 3,015)
Age (year)	39.4 ± 0.34	41.1 ± 0.29
Family income, lower middle or less (%)	586 (29.6)	943 (30.0)
Higher education (%)[a]	1,002 (51.6)	1,295 (44.0)
Current smoker (%)	756 (38.7)	159 (6.07)
Current alcohol consumer (%)	1,527 (77.7)	1,508 (52.4)
Regular exercise (%)[b]	1,086 (57.3)	1,460 (50.9)
Postmenopausal women (%)	—	977 (27.7)
Body mass index (kg/m^2)	24.6 ± 0.09	22.9 ± 0.08
Waist circumference (cm)	85.8 ± 0.23	77.0 ± 0.22
Dietary intake		
Energy intake (kcal/day)	2,334 ± 19.4	1,746 ± 13.1
Modified Korean Healthy Eating Index[c]	48.7 ± 0.41	54.8 ± 0.36
Beverage consumption (servings/week)		
Total coffee	8.89 ± 0.26	7.44 ± 0.19
Non-sugar sweetened coffee	3.95 ± 0.24	4.35 ± 0.18
Sugar sweetened coffee	4.93 ± 0.19	3.09 ± 0.12
Green tea	0.98 ± 0.08	0.61 ± 0.05
Fruit juice/drink (excluding homemade)	0.78 ± 0.04	0.46 ± 0.03
Soda	1.64 ± 0.07	0.70 ± 0.04

All values accounted for the complex sampling design effect of the national surveys using PROC SURVEY procedure, and values are expressed as the mean ± SE or number (%). [a]≥college (12 years of education). [b]≥75 min/week of vigorous-intensity physical activity or ≥150 min/week of moderate-intensity physical activity. [c]Modified Korean Healthy Eating Index score ranged from 0 (non-adherence) to 100 points (perfect adherence).

positive association between soda consumption and elevated hs-CRP (OR = 1.79, 95% CI = 1.23–2.61; p-trend = 0.013). In men, an inverted J-shaped association was found between commercial fruit juice/drink consumption and elevated hs-CRP. There were no significant associations of NSS-coffee, SS-coffee, and green tea with elevated hs-CRP in both men and women.

After stratified by obesity status (Table 3), the inverse associations of total coffee with elevated hs-CRP status was found in obese women (OR = 0.31, 95% CI = 0.15–0.65 for total coffee consumers and both p_{trend} <0.05 in obese women by BMI and WC), but no significant interaction. An additional inverse association with hs-CRP status was found in green tea in obese women (OR = 0.48, 95% CI = 0.23–0.99 in WC ≥85 cm; p_{inter} <0.05 for both obesity status by BMI and WC for green tea). A positive association between soda consumption and hs-CRP status remained only in obese women (OR = 2.21, 95% CI 1.22–4.02 in BMI ≥25 kg/m^2 and OR = 3.14, 95% CI 1.62–6.08 in WC ≥85 cm; p_{inter} <0.05 for both obesity status by BMI and WC for soda). In men, we found positive associations between fruit juices/drinks and hs-CRP status in obese men by BMI and WC (OR = 2.44, CI = 1.44–4.16, p_{trend}<0.05 in BMI ≥25 kg/m^2; OR = 2.31, 1.27–4.19, p_{trend} >0.05 in WC ≥90 cm).

In only SS-coffee and only NSS-coffee analyses (Table 4), both SS-coffee and NSS-coffee were inversely associated with elevated hs-CRP status in abdominally obese women (OR = 0.49, 95% CI = 0.25–0.99 in only SS-coffee, and OR = 0.45, 95% CI = 0.21–0.94 in only NSS-coffee), although there were no significant interactions between coffee and obesity (all p_{inter} >0.05).

Discussion

Among NABs, coffee consumption was inversely and soda was positively associated with elevated hs-CRP status in women. After stratifying for obesity, these inverse and positive associations were identifiable only in obese women. In the case of coffee, these results were also found for both SS-coffee and NSS-coffee. Green tea consumption was also inversely associated with hs-CRP status in obese women. In men, only commercial fruit juice/drink consumption was positively associated with elevated hs-CRP status and this adverse association was found only in obese men.

Coffee, after water, was reported as the most consumed beverage worldwide.[34] A report from the US National Coffee Association in 2017, 62% of adults drank coffee daily.[35] Similarly, 64.0% of participants in the present study drank coffee daily. Tea, which accounts for 20% of total tea consumption worldwide, is consumed primarily in some Asian countries including Korea, China, Japan, and India.[36] In the present study, 15.3% of participants consumed green tea more than once per week and 18.5% consumed fruit drinks more than once per week. For soda, about 50% of Americans adults daily consumed soda (2.6 glasses/day).[37] Koreans consumed lower quantities of SSBs than Western populations and in the present study, the proportion of consumers having more than one glass of soda per week (2.2 glasses/week) was only 30.2%.[38] Nevertheless, SSBs consumption has been steadily increasing in Korea and then it has almost doubled over an 11-year period between 1998 and 2009.[39] This increasing phenomenon of SSBs consumption has become a health concern in most countries over the past decades because SSBs consumption accounts for a substantial portion of total energy intake.[6,8] The consumption of total commercial fruit beverages increased by 23% between 2003 and 2018, globally, but among those beverages, 100% fruit juice decreased by more than 10%.[40] This phenomenon was also observed in Korea and fruit drinks accounted for 82.0% of total fruit beverage consumption and only 18.0% was 100% fruit juice in 2017.[41]

The first finding in the present study was the inverse association between coffee consumption and hs-CRP. This inverse association was consistent with the findings of a recent meta-analysis of cross-sectional studies, although there was lack of long-term

Table 2. Weighted and age-adjusted characteristics of the study participants according to total coffee consumption

Total coffee	Men (n = 1,984)					Women (n = 3,015)				
	Never or almost never	≥1/month to <1/day	≥1/day	p_{diff}[d]	p_{trend}[e]	Never or almost never	≥1/month to <1/day	≥1/day	p_{diff}[d]	p_{trend}[e]
n	241	562	1,181	—	—	428	1,014	1,573	—	—
Median serving per week	0	2.47	9.84	—	—	0	3.02	9.07	—	—
Age (year)	34.5 ± 0.89[a]	36.7 ± 0.59[a]	41.9 ± 0.37[b]	<.001	<.001	36.8 ± 0.82[a]	40.6 ± 0.49[b]	42.7 ± 0.36[c]	<.001	<.001
Family income, lower middle or less (%)	33.4	30.4	27.8	0.181	0.081	36.5[a]	32.5[a]	26.3[b]	<.001	<.001
Higher education (%)[a]	44.8[a]	46.7[a]	55.9[b]	<.001	<.001	35.9[a]	39.7[a]	50.1[b]	<.001	<.001
Current smoker (%)	25.4[a]	29.8[a]	45.8[b]	<.001	<.001	4.00[ab]	3.20[a]	8.40[b]	<.001	<.001
Current alcohol consumer (%)	68.8[a]	78.6[b]	79.1[b]	0.006	0.033	36.5[a]	52.1[b]	58.7[c]	<.001	<.001
Regular exercise (%)[b]	57.3	60.8	54.9	0.138	0.097	52.0	50.1	51.6	0.735	0.776
Postmenopausal women (%)	—	—	—	—	—	38.3[a]	30.0[b]	22.4[c]	<.001	<.001
Body mass index (kg/m²)	23.8 ± 0.25[a]	24.6 ± 0.19[ab]	24.9 ± 0.11[b]	0.001	0.001	22.2 ± 0.20[a]	23.0 ± 0.13[b]	23.0 ± 0.09[b]	0.001	0.010
Waist circumference (cm)	83.5 ± 0.61[a]	86.0 ± 0.48[b]	86.4 ± 0.29[b]	<.001	<.001	75.4 ± 0.52[a]	77.2 ± 0.34[b]	77.1 ± 0.26[b]	0.005	0.035
Dietary intake										
Energy intake (kcal/day)	2,193 ± 55.9[a]	2,263 ± 37.0[a]	2,382 ± 26.0[b]	0.001	<.001	1,678 ± 34.3[a]	1,707 ± 20.8[a]	1,802 ± 19.5[b]	<.001	<.001
Modified Korean Healthy Eating Index[c]	47.6 ± 0.87[ab]	48.8 ± 0.59[a]	45.5 ± 0.45[b]	<.001	<.001	59.4 ± 0.77[a]	57.4 ± 0.52[b]	56.3 ± 0.41[b]	<.001	<.001
Beverage consumption (servings/week)										
Non-sugar sweetened coffee	0.00 ± 0.13	0.62 ± 0.12	6.60 ± 0.42	—	—	0.00 ± 0.14	0.99 ± 0.11	7.57 ± 0.28	—	—
Sugar sweetened coffee	0.27 ± 0.09	1.65 ± 0.10	7.90 ± 0.27	—	—	0.50 ± 0.11	1.75 ± 0.11	5.64 ± 0.25	—	—
Green tea	0.96 ± 0.21	1.00 ± 0.17	0.95 ± 0.11	0.971	0.850	0.71 ± 0.17	0.71 ± 0.08	0.67 ± 0.06	0.888	0.674
Fruit juice/drink (excluding homemade)	0.82 ± 0.15	0.72 ± 0.07	0.56 ± 0.05	0.077	0.029	0.72 ± 0.11	0.60 ± 0.06	0.54 ± 0.04	0.158	0.060
Soda	1.25 ± 0.16	1.37 ± 0.11	1.37 ± 0.08	0.828	0.711	0.70 ± 0.08[a]	0.96 ± 0.07[b]	0.83 ± 0.06[ab]	0.017	0.834

KHEI, Korean Healthy Eating Index. All results were adjusted for age, and KHEI and beverage consumption were adjusted for age and total energy intake. [a]≥college (12 years of education). [b]≥75 min/week of vigorous-intensity physical activity or ≥150 min/week of moderate-intensity physical activity. [c]Modified Korean Healthy Eating Index score ranged from 0 (non-adherence) to 100 points (perfect adherence). [d]*p* for differences were determined by the general linear model (GLM). Mean values with different superscripts (a, b, c) within a row were significantly different among the three groups on Tukey's multiple comparison test. [e]*p* for trends were obtained by imputing the median value of each group and treating it as a continuous variable.

Table 3. Multivariable-adjusted ORs and 95% CI between non-alcoholic beverages (NABs) consumption and elevated levels of hs-CRP by obesity status

NABs	Men (n = 1,984)					Women (n = 3,015)				
	Never or almost never (ref)	≥1/month to <1/day (coffee) or <1/week (others)	≥1/day (coffee) or ≥1/week (others)	p_{trend}	p_{inter}	Never or almost never (ref)	≥1/month to <1/day (coffee) or <1/week (others)	≥1/day (coffee) or ≥1/week (others)	p_{trend}	p_{inter}
Total coffee										
n	241	562	1,181			428	1,014	1,573		
Age-adjusted model	1.00 (ref)	0.86 (0.50–1.50)	1.08 (0.62–1.86)	0.372	—	1.00 (ref)	1.21 (0.77–1.91)	0.90 (0.59–1.36)	0.102	—
Multivariable model[a]	1.00 (ref)	0.73 (0.42–1.28)	0.83 (0.47–1.46)	0.989	—	1.00 (ref)	1.01 (0.64–1.60)	0.70 (0.44–1.09)	0.014	—
Stratified by obesity status										
BMI, <25	1.00 (ref)	0.97 (0.46–2.05)	0.85 (0.40–1.85)	0.588	0.369	1.00 (ref)	1.34 (0.71–2.53)	0.98 (0.52–1.83)	0.394	0.258
≥25	1.00 (ref)	0.50 (0.23–1.10)	0.75 (0.37–1.55)	0.640		1.00 (ref)	0.68 (0.36–1.31)	0.44 (0.22–0.90)	0.014	
WC, <90 in men, 85 in women	1.00 (ref)	1.10 (0.55–2.20)	1.02 (0.51–2.04)	0.889	0.053	1.00 (ref)	1.32 (0.72–2.43)	1.09 (0.60–2.00)	0.746	0.062
≥90 in men, 85 in women	1.00 (ref)	0.28 (0.11–0.73)	0.54 (0.22–1.34)	0.668		1.00 (ref)	0.58 (0.28–1.22)	0.31 (0.15–0.65)	0.001	
Green tea										
n	1,325	303	356			2,226	399	390		
Age-adjusted model	1.00 (ref)	1.44 (0.98–2.09)	1.08 (0.72–1.61)	0.848	—	1.00 (ref)	0.79 (0.48–1.29)	1.00 (0.68–1.47)	0.945	—
Multivariable model[b]	1.00 (ref)	1.42 (0.97–2.09)	1.10 (0.73–1.66)	0.805	—	1.00 (ref)	0.80 (0.49–1.32)	0.91 (0.60–1.38)	0.675	—
Stratified by obesity status										
BMI, <25	1.00 (ref)	1.60 (0.86–2.96)	0.77 (0.38–1.58)	0.376	0.537	1.00 (ref)	1.16 (0.64–2.09)	1.28 (0.77–2.13)	0.357	0.048
≥25	1.00 (ref)	1.32 (0.79–2.21)	1.32 (0.78–2.23)	0.341		1.00 (ref)	0.44 (0.20–0.97)	0.61 (0.33–1.14)	0.127	
WC, <90 in men, 85 in women	1.00 (ref)	1.58 (0.90–2.75)	0.97 (0.56–1.68)	0.747	0.738	1.00 (ref)	1.06 (0.59–1.91)	1.29 (0.81–2.05)	0.280	0.044
≥90 in men, 85 in women	1.00 (ref)	1.22 (0.70–2.13)	1.28 (0.69–2.36)	0.443		1.00 (ref)	0.44 (0.18–1.07)	0.48 (0.23–0.99)	0.049	
Fruit juice/drink (excluding homemade)										
n	1,015	527	442			2,014	638	363		
Age-adjusted model	1.00 (ref)	1.83 (1.27–2.64)	1.56 (1.04–2.32)	0.042	—	1.00 (ref)	1.37 (0.99–1.89)	1.38 (0.95–2.02)	0.081	—
Multivariable model[c]	1.00 (ref)	1.84 (1.28–2.66)	1.48 (0.98–2.25)	0.092	—	1.00 (ref)	1.33 (0.95–1.86)	1.15 (0.78–1.70)	0.474	—
Stratified by obesity status										
BMI, <25	1.00 (ref)	1.62 (0.95–2.78)	0.82 (0.45–1.49)	0.306	0.014	1.00 (ref)	1.19 (0.74–1.92)	1.34 (0.76–2.35)	0.281	0.378
≥25	1.00 (ref)	2.16 (1.36–3.44)	2.44 (1.44–4.16)	0.001		1.00 (ref)	1.42 (0.87–2.29)	0.82 (0.42–1.62)	0.611	
WC, <90 in men, 85 in women	1.00 (ref)	1.75 (1.06–2.87)	1.19 (0.69–2.05)	0.766	0.062	1.00 (ref)	1.18 (0.76–1.84)	1.38 (0.84–2.29)	0.181	0.246
≥90 in men, 85 in women	1.00 (ref)	2.05 (1.20–3.49)	2.31 (1.27–4.19)	0.011		1.00 (ref)	1.49 (0.88–2.52)	0.88 (0.39–1.96)	0.776	
Soda										
n	791	486	707			1,844	639	532		
Age-adjusted model	1.00 (ref)	1.29 (0.87–1.91)	1.15 (0.76–1.72)	0.858	—	1.00 (ref)	2.13 (1.55–2.93)	2.02 (1.42–2.88)	0.001	—
Multivariable model[d]	1.00 (ref)	1.19 (0.80–1.76)	0.97 (0.64–1.46)	0.552	—	1.00 (ref)	2.08 (1.50–2.87)	1.79 (1.23–2.61)	0.013	—
Stratified by obesity status										
BMI, <25	1.00 (ref)	1.21 (0.66–2.21)	0.89 (0.45–1.76)	0.520	0.400	1.00 (ref)	1.24 (0.74–2.07)	1.29 (0.80–2.08)	0.350	0.005
≥25	1.00 (ref)	1.18 (0.69–2.02)	0.93 (0.53–1.62)	0.545		1.00 (ref)	2.70 (1.65–4.42)	2.21 (1.22–4.02)	0.053	
WC, <90 in men, 85 in women	1.00 (ref)	1.30 (0.75–2.26)	1.11 (0.61–2.02)	0.996	0.689	1.00 (ref)	1.33 (0.85–2.06)	1.15 (0.71–1.87)	0.706	<.001
≥90 in men, 85 in women	1.00 (ref)	1.07 (0.57–2.01)	0.69 (0.37–1.30)	0.148		1.00 (ref)	3.19 (1.87–5.46)	3.14 (1.62–6.08)	0.026	

BMI, body mass index (kg/m^2); WC, waist circumference (cm); KHEI, Korean Healthy Eating Index. Data are expressed as OR (95% CI). The definition of obesity is a BMI ≥25 kg/m^2 and that of abdominal obesity is a WC ≥90 cm in men and ≥85 cm in women. Multivariable model: adjusted for age, socio-economic confounders, dietary intake (energy and KHEI), and consumption of different types of NABs (by NAB and gender). *P* for linear trend was determined by treating the median value of each group as a continuous variable using logistic regression and *p* interactions with obesity status were tested using a cross-product term in multivariable model with NABs. [a]Multivariable model was adjusted for age, education, smoking status, alcohol consumption, WC, energy, fruit juice/drink, and modified KHEI for men, and was adjusted for age, income, education, smoking status, alcohol consumption, menopausal status, BMI, energy, soda and modified KHEI for women. [b]Multivariable model was adjusted for age, income, education, energy, SS-coffee, soda, and modified KHEI for men, and was adjusted for age, income, education, physical activity, BMI, energy, NSS-coffee, SS-coffee, and modified KHEI for women. [c]Multivariable model was adjusted for age, energy, soda, and modified KHEI for men, and was adjusted for age, income, menopausal status, energy, and soda for women. [d]Multivariable model was adjusted for age, education, physical activity, energy, fruit juice/drink, and modified KHEI for men, and was adjusted for age, income, menopausal status, energy, NSS-coffee, sugar sweetened coffee, fruit juice/drink, green tea, and modified KHEI for women.

Table 4. Multivariable-adjusted ORs and 95% CIs of elevated levels of hs-CRP according to the type of coffee consumption

Type of coffee consumed	Men (n = 1,984)					Women (n = 3,015)				
	Never or almost never	Only SS-coffee consumer	Both types of coffee consumer	Only NSS-coffee consumer	p_{inter}	Never or almost never	Only SS-coffee consumer	Both types of coffee consumer	Only NSS-coffee consumer	p_{inter}
n	241	1,080	320	343		428	1,153	654	780	
Age-adjusted model	1.00 (ref)	1.02 (0.59–1.78)	1.07 (0.59–1.95)	0.89 (0.48–1.64)	—	1.00 (ref)	1.17 (0.74–1.84)	0.97 (0.6–1.54)	0.89 (0.56–1.42)	—
Multivariable model[a]	1.00 (ref)	0.93 (0.52–1.64)	1.06 (0.57–1.96)	0.94 (0.50–1.75)	—	1.00 (ref)	1.06 (0.65–1.71)	1.03 (0.63–1.68)	0.97 (0.60–1.56)	—
Stratified by obesity status										
BMI, <25	1.00 (ref)	0.93 (0.43–2.01)	0.96 (0.39–2.36)	0.76 (0.33–1.76)	0.881	1.00 (ref)	1.41 (0.73–2.74)	1.07 (0.50–2.30)	1.09 (0.57–2.11)	0.311
≥25	1.00 (ref)	0.83 (0.42–1.64)	1.02 (0.47–2.25)	0.88 (0.41–1.90)		1.00 (ref)	0.64 (0.33–1.24)	0.66 (0.33–1.31)	0.60 (0.30–1.18)	
WC, <90 in men, 85 in women	1.00 (ref)	1.05 (0.52–2.10)	1.32 (0.60–2.92)	0.92 (0.41–2.07)	0.183	1.00 (ref)	1.44 (0.77–2.69)	1.18 (0.58–2.40)	1.18 (0.64–2.18)	0.137
≥90 in men, 85 in women	1.00 (ref)	0.49 (0.22–1.11)	0.50 (0.19–1.32)	0.51 (0.20–1.27)		1.00 (ref)	0.49 (0.25–0.99)	0.53 (0.25–1.09)	0.45 (0.21–0.94)	

NSS, Non-sugar sweetened; SS, Sugar-sweetened; BMI, body mass index (kg/m^2); WC, waist circumference (cm); KHEI, Korean Healthy Eating Index. Data are expressed as OR (95% CI). *P* interactions with obesity status were tested using a cross-product term in multivariable model with the type of coffee consumption. [a]Multivariable model was adjusted for age, income, education, smoking status, alcohol consumption, energy, soda and modified KHEI for men and was adjusted for age, income, education, smoking status, alcohol consumption, physical activity, menopausal status, energy, soda, and modified KHEI for women.

trials with large size samples.[12] A hormone replacement therapy trial among US postmenopausal overweight/obese women reported an attenuated association between BMI and CRP by coffee consumption, which was in the same line with our findings that the inverse association remained only in obese women. In the present study, the inverse association shown only in obese women was observed for not only NSS-coffee but also SS-coffee. Although there was no significance in coffee consumers of both types, there was very similar tendency. A recent review study suggested that added sugar of coffee may attenuate the protective effect of coffee on cardiometabolic conditions such as lipid profiles, because it may play a role as an important confounder for the association of coffee with them, particularly over five cups of SS-coffee.[42] However, we could not classify participants into over five cups of SS-coffee/day group due to sample size. Moreover, since SS-coffee consumption was highly correlated with sugar intake (r>0.90), we could not adjust for sugar intake in the analysis of the type of coffee consumption. Therefore, we could not assert that SS-coffee is beneficial for hs-CRP regardless of sugar content. We found another inverse association with hs-CRP status in green tea in obese women. Antioxidant properties of green tea including flavonoids, catechins, and caffeine in green tea were previously postulated to reduce hs-CRP status, but there was no consistent beneficial effect in a meta-analysis of RCT.[11] In the present study, there were some limitations to analyze green tea and hs-CRP; green tea was not differentiated from other types of tea, and moreover, SS-tea and NSS-tea were not distinguishable. Therefore, further research is necessary to clarify the nature of the association between specific-tea consumption and hs-CRP.

The link between SSBs such as soda and fruit juice and elevated CRP has been examined in a cross-sectional study of US women nurses (Nurses' Health Study, NHS),[10] a study of US health professional men,[43] and a Mexican women teachers study.[32] Like our findings in women, SSBs were positively associated with hs-CRP status in a dose-dependent manner in the NHS study.[10] In the Mexican women teachers study, women in the highest quartile of soda consumption had a 50% higher CRP level than those in the lowest quartile of soda consumption.[32] Although there was little evidence on overall fruit juices/drinks to compare with our findings, the findings in women in the NHS and men from the US health professional study were similar to our findings; there was no significant association between fruit juice and CRP in women.[10] but the US health professional men study demonstrated that one serving per day increase in fruit drinks consumption was associated with a 25% increase in the levels of several inflammatory factors including CRP.[43]

We found a sex difference in the association with hs-CRP in the present study, particularly for soda and fruit juices/drinks. As for coffee, there was no significant association in men, but the association tendency is similar between men and women. Thus, there may not be sex-difference for coffee and green tea. A possible explanation for sex-difference in soda and commercial fruit juices/drinks is that sex hormones may modulate the metabolic response of diet, and their role might be dependent on sugar profiles.[44,45] However, until now, biological mechanisms underlying the associations between the consumption of a specific NAB and sex have rarely been demonstrated.

There are several possible mechanisms in the relationship between NAB consumption and hs-CRP status. First, coffee contains more than 100 chemical components including caffeine, polyphenols, and minerals.[13,14] Green tea is a food rich in polyphenol flavonoids including catechin, gallocatechin, epigallocatechin, epicatechin gallate, and epigallocatechin 3-gallate, which has the ability of scavenging free radicals species.[46] These were suggested to be responsible for the antioxidants and anti-inflammatory effects of coffee and tea.[11,12,15] Second, SSBs such as soda have a low satiating effect through provision of liquid calories; therefore, SSB drinkers may subsequently have more energy.[8] Also, consumption of SSBs including soda, which contains rapidly absorbable sugar, has been shown to result in rapid increases in blood glucose and insulin concentrations.[8] This property, high glycemic index (GI), is suggested to be associated with elevated inflammation levels.[47] Commercial fruit/vegetable juices have these properties and cannot be recommended as a healthy substitute or alternative.[48] Finally, the stronger associations with elevated hs-CRP in the obese group may be explained by the fact that obesity predisposes individuals to a pro-inflammatory state via increased inflammatory mediator interleukin-6 (IL-6).[49] This increase in IL-6 may trigger the hepatic synthesis of CRP and TNF-α (tumor necrosis factor alpha) and reduce levels of adiponectin.

The present study had some limitations. First, although this study data was from a large representative population, it was a cross-sectional study design. Therefore, we could not establish causal links between NAB consumption and hs-CRP status. The associations of specific NABs with hs-CRP in the present study should be confirmed in large-scale prospective studies. Second, dietary data of the KNHANES were self-reported; thus potential recall and nonresponse biases remained. Third, the FFQ was not specifically developed for a study on NABs; therefore, the FFQ did not collect data on all kinds of beverages separately. Because different types of beverages were included in one question, sugar-added type and sugar-free type were not distinguishable for green tea and commercial fruit juice/drinks. Finally, NAB consumption may be correlated with other dietary patterns or unmeasured covariates which may affect hs-CRP levels. To display possible relationships with other foods consumed, we demonstrated radar charts in Supplemental Fig. 1*. For example, in women, participants with high green tea consumption tended to have high seaweed consumption. Participants with high SSB such as commercial fruit juice/drink and soda tended to have relatively high meat, poultry, and carbohydrate-rich foods such as snacks and ice cream, rice cake, and bread/noodles/cereal, but low multi-grain rice and fish and seafood. However, adjusting those food groups in place of the modified KHEI did not substantially change the associations.

In conclusion, coffee and green tea consumption was cross-sectionally inversely associated with elevated hs-CRP status and that soda in women and commercial fruit juice/drinks in men were positively associated with elevated hs-CRP status, particularly in the obese population. However, for the adequate recommendation of NABs to the public, further studies should be needed considering the types of NABs, sugar content, and obesity status in the large-size prospective studies.

Author Contributions

Conceptualization: MKK. Formal analysis: JSK and HWW. Methodology: JSK, MKK, and HWW. Writing - original draft: JSK and MKK. Writing - review and editing: JSK, MKK, and YMK. The authors received no specific funding for this work. The authors do not have any conflicts of interest associated with this manuscript to report.

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Conflict of Interest

No potential conflicts of interest were disclosed.

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