



The association between sugar-sweetened beverages intake, body mass index, and inflammation in US adults

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Abstract

Objectives This study aims to (1) assess the associations between sugar-sweetened beverages (SSB) consumption and C-reactive protein (CRP) levels, and (2) evaluate the modifying effect of body mass index (BMI) on the association between SSB consumption and CRP levels.

Methods A total of 6856 eligible adults were selected from the 2007–2010 National Health and Nutrition Examination Survey (NHANES). Average quantity of SSB consumption was calculated from 2-day 24-h dietary recalls. All data analyses were performed with appropriate sampling weights.

Results Compared with non-SSB drinkers, a 0.26 mg/l higher CRP was observed in heavy SSB drinkers after adjusting for demographic characteristics, lifestyle patterns, and BMI. An effect modification of BMI on SSB intake and CRP levels was detected ($P < 0.05$). Medium and heavy SSB consumers with obesity had 0.58 and 0.50 higher CRP than non-SSB consumers, respectively ($P = 0.014$ and 0.013). No association was found in SSB drinkers who were normal weight or overweight.

Conclusions These findings emphasize that SSB intake is positively associated with CRP levels. Obesity might strengthen CRP levels in individuals with medium/heavy amount of SSB consumption.

Keywords Sugar-sweetened beverages · Inflammation · C-reactive protein · Body mass index · NHANES

Introduction

The positive association between added sugar consumption and the development of numerous metabolism-related diseases—including obesity, diabetes, and cardiovascular

disease in adults—is well documented (Malik et al. 2010). According to a US population survey, sugar-sweetened beverages (SSB) are the primary source of excessive intake of added sugar, especially in adolescents and young adults (Marriott et al. 2009). Recent publications from the 2011–2014 National Health and Nutrition Examination Survey (NHANES) report that the average caloric consumption from SSB among male and female adults was 179 and 113 kcal per day, respectively (Rosinger et al. 2017). These findings indicate that approximately 50% of US adults consume at least one serving of SSB per day (Rosinger et al. 2017). From 1990 to 2008, NHANES found a decline in the prevalence of SSB intake in US adults (Welsh et al. 2011), but excess caloric consumption from SSB remained higher than the 10% of daily total energy intake recommended by the World Health Organization (WHO) (The World Health Organization 2015). The prevalence of obesity also significantly increased, from 30.5 to 39.6%, in US adults during this same time period (Hales et al. 2017). Furthermore, the prevalence of

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overweight or obese male and female adults in the USA in 2013–2014 was 73.7% and 66.9%, respectively (Centers for Disease Control and Prevention. Overweight & Obesity Statistics). Thus, excessive BMI remains a vital health issue that will affect future health problems in the US population.

C-reactive protein (CRP), a pro-inflammatory cytokine, is produced and secreted by interleukin-6 (IL-6) stimulating hepatocytes, and its concentration also varies in endothelial cells, smooth muscle cells, and adipose tissue (Zhang et al. 2009). A raised concentration of pro-inflammatory cytokines is associated with increased adiposity (Rodriguez-Hernandez et al. 2013). The American Heart Association (AHA) and the Centers of Disease Control and Prevention (CDC) have both proposed that obesity and elevated CRP levels are closely related to the risk of future heart disease and suggest that CRP should be considered as a vital risk factor for cardiovascular disease (Meguro et al. 2012). Consistently, individuals who are overweight/obese, have type 2 diabetes, and/or have cancer exhibit significantly increased concentrations of CRP (Asgar and Sheikh 2017; Rodriguez-Hernandez et al. 2013; Unamuno et al. 2018). Additionally, inflammatory biomarkers may vary across many demographic characteristics, including aging, race, socioeconomic status, dietary patterns, and individual lifestyle patterns (Alley et al. 2006; O'Connor and Irwin 2010; Paalani et al. 2011; Singh and Newman 2011).

Recently, some studies have found a positive association between SSB consumption and elevated CRP concentration in a diverse of group study subjects, even after controlling for potential confounders (Aeberli et al. 2011; Hert et al. 2014; Schulze et al. 2005; Tamez et al. 2018; Yu et al. 2018). However, these studies used limited and inconsistent estimations of SSB consumption and only a few controlled for BMI level. Those adjusting for BMI reported a positive association, even after adjusting for BMI (Tamez et al. 2018; Yu et al. 2018). To date, no study has explored whether the association between SSB intake and inflammation differs among a large population with varying BMI status.

The purpose of this study is to investigate the association between the quantities of SSB consumption and CRP levels in a national sample of the US adult population. We further assessed the effects of the quantity of SSB consumption on CRP level among normal weight, overweight, and obese individuals.

Methods

Study population

National Health and Nutrition Examination (NHANES), a continuous US nationwide population-based survey

conducted by the Centers for Disease Control and Prevention (National Center for Health Statistics), was used in this study. Our study subjects were selected from two 2-year cycles of 2007–2008 and 2009–2010 due to two available data limitations. The first limitation is that CRP levels were not detected after cycle 2011–2012. Therefore, the most recent available data come from cycle 2009–2010. Furthermore, physical activity data collection was changed during cycle 2005–2006 and cycle 2007–2008. The Global Physical Activity Questionnaire (GPAQ) was started using to obtain physical activity information in 2007–2008. Therefore, cycle 2007–2008 and cycle 2009–2010 are the most recent available data of NHANES that can be used to investigate our study objectives. NHANES was performed by using a multistage probability and stratified sampling method to represent the national US population (the Centers for Disease Control and Prevention). Participants 20 years of age or older who completed a 24-h dietary recall interview, as well as anthropometric and biochemical examinations, were selected for this study. To consider limited sugar consumption in diabetic patients and people with special diets or people had extremely high daily total caloric intake may have high sugar intake that affect SSB consumption pattern and inflammation, we excluded 1186 diabetic patients, 816 special diet consumers (including low calorie, low fat, sugar-free, diabetic, weight gain, low carbohydrate, high protein, and others), and 69 extremely high total energy consumers (> 5000 kcal/day). Differences in background characteristics, SSB consumption, and inflammation status were also examined based on our selection criteria. A total of 6856 eligible adults with both CRP and BMI measurements were included in the final analysis. The research protocol was reviewed and approved by the Institutional Review Board at the National Center for Health Statistics before data collection. Informed consent was signed by each study participant (National Center for Health Statistics).

Measurements

Twenty-four-hour dietary recall interviews on two non-consecutive days were conducted both at home and in mobile examination centers (MEC) by trained research staff in order to obtain daily dietary and estimated daily total energy intake (the Centers for Disease Control and Prevention). Beverages with added sugars by manufacturers—including soft drinks, sport drinks, energy drinks, fruit-flavored sweetened drinks, artificial fruit juices, sweetened teas and coffees, and other sweetened drinks (such as regular energy drinks and traditional sweetened drinks)—were considered SSB in this study. Nutritional

information for each food item and food components in NHANES was calculated and transformed to USDA codes by research staff. In this study, we identified each sugary drink with added sugar consumption based on suggested food codes from the United States Department of Agriculture (USDA) Food and Nutrient Database for Dietary Studies (Mesirow and Welsh 2015). An average amount of SSB consumption per day (ml/day) was generated from 24-h dietary recall interviews. To understand how the amounts of SSB intake associate with inflammation, the total amount of SSB intake was further categorized into non-SSB intake, 1–350 (light), 351–699 (medium), and ≥ 700 ml/day (heavy), based on one can of soda (355 ml) based on the amount of one can of soda. Total energy intake (kcal/day) was also estimated from the 2-day 24-h dietary recall interviews.

Blood specimens were collected via venipuncture at MEC after participants completed questionnaire interviews (National Center for Health Statistics; National Center for Health Statistics). Detailed procedures and analytic methods are described in the NHANES Description of Laboratory Methodology section. To avoid the effect of acute infection associated with abnormal increased inflammation, we excluded a total of 1007 study subjects who had a CRP concentration greater than 10 mg/l (Knight 2015).

Height and body weight measurements obtained from standardized physical examinations were used to calculate BMI. According to the CDC definition of BMI criteria for adults ≥ 20 years old, participants with BMI values of < 25 , 25–29.9, and ≥ 30 kg/m² were defined as normal weight, overweight, and obese, respectively (the Centers of Disease Control and Prevention).

Data on personal characteristics and lifestyle patterns were collected using structural questionnaires (the Centers for Disease Control and Prevention). Demographic and socioeconomic characteristics such as age, gender, race, and poverty income ratio (PIR) were considered as potential confounders. Substance use included cigarette smoking and alcohol use status. Based on the questionnaire used in NHANES, individuals were identified as non-smokers (less than 100 cigarettes/lifetime), former, or current smokers (current smoking status). Alcohol drinking status, which was obtained from three questions, identified participants as non-alcohol drinkers (< 12 drinks/lifetime), light (≥ 12 drinks/past year and ≤ 5 drinks/day), or heavy (≥ 12 drinks/past year and > 5 drinks/day).

Level of weekly physical activity was calculated by determining number of days in a week engaged in vigorous-/moderate-intensity sports or fitness or recreational activities, and time spent doing vigorous-/moderate-intensity sports or fitness or recreational activities per day. According to the WHO recommendation of physical activity for adults, adequate physical activity was

categorized as at least 150 min of moderate-intensity activities or at least 75 min of vigorous-intensity activities during leisure time per week (WHO 2004).

Data on personal health conditions and medical history were obtained from a self-reported interview. Participants with asthma, chronic bronchitis, emphysema, heart diseases, gout, arthritis, stroke, coronary heart disease, angina, heart failure, heart attack, anemia, any liver condition, and multiple types of cancer were classified as having a chronic disease.

Statistical analysis

To adjust for the complex multistage and oversampling study design of NHANES, appropriate sampling weights were selected, and average sampling weights were calculated according to the NHANES Survey Methods and Analytic Guideline on the Web site (National Center for Health Statistics). Sampling weights were applied in all analyses (National Center for Health Statistics) to adjust for the complex multistage and oversampling study design of NHANES. To summarize the distribution of participants' demographic factors, lifestyle patterns, substance use, personal medical history, and BMI status were summarized using unweighted sample size (n) and weighted percentage (%). The difference in CRP levels between participants' characteristics, including demographic factors, lifestyle patterns, substance use, personal medical history, and BMI status, was described using mean \pm SE under F -test. The associations between amount of SSB intake and CRP levels with and without adjusting for the potential confounders were evaluated using univariate (Model 1) and multivariable linear regression models (Model 2), respectively. Model 3 (additionally adjusted for BMI status) was performed to examine how BMI status affects the association SSB intake and CRP levels. Potential confounders, such as age, gender, ethnicity, PIR, cigarette smoking, alcohol drinking, physical activity, personal diseases, total energy intake, and BMI, were decided by the significant effect of personal characteristics on CRP levels and prior studies suggested. Multivariable model with interaction term of SSB consumption and BMI status was used to test whether BMI status (BMI 25–29.9 and ≥ 30 kg/m² was defined as overweight and obesity, respectively) modified the association between amount of SSB consumption and CRP level. Finally, a stratified analysis was performed to examine the different association between the amount of SSB consumption and CRP levels among those who were normal weight, overweight, and obese. All statistical analyses were performed under survey data modules using Stata software (Stata version 14, StataCorp., College Station, TX, USA), and statistical significance was determined using a two-tailed p value ≤ 0.05 .

Results

Table 1 shows the weight-adjusted distributions of CRP levels by demographic characteristic, substance use, physical activity, self-reported diseases, BMI status, and SSB consumption. Higher CRP levels were found in individuals who were older, female, non-Hispanic black, had lower PIR, were current smokers, had low physical activity, had self-reported chronic disease, had high amount of SSB intake, and were obese (all P 's ≤ 0.047).

Table 2 presents univariate regression models and multivariate-adjusted differences in amount of SSB intake, BMI, and individual characteristics related to CRP levels. In the univariate models (Model 1), higher levels of CRP were found in populations who were heavy SSB consumers (≥ 700 ml/day), of older age (50–80 years old), female, non-Hispanic black/other race, current cigarette smokers, heavy alcohol drinkers, and had chronic disease (all P 's ≤ 0.024). Higher PIR (200–299%, 300–399%, and above 400%), adequate weekly physical activity, and daily dietary intake > 100 kcal were associated with reduced CRP concentrations (P 's ≤ 0.020 in PIR, $P < 0.001$ for physical activity, and $P < 0.001$ for total energy intake). Study subjects who were overweight or obese had a 0.66–1.85 higher CRP level than the normal weight population (all P 's < 0.001). After adjusting for covariates in Model 1, the augmented impact of heavy SSB intake on higher CRP was analyzed. Individuals consuming the highest amount of SSB (≥ 700 ml/day) were more like to have increased CRP levels (aDiff. = 0.31 mg/l, $P = 0.013$). In order to consider the contribution of BMI on inflammation, we additionally adjusted for BMI status in Model 3. When compared to non-SSB consumers, heavy SSB consumers (≥ 700 ml/day) had a 0.26 mg/l significantly higher CRP level ($P = 0.016$). The significant interacting effect of BMI and SSB consumption on CRP level was detected in obese, medium SSB consumers (aDiff. = 0.51 mg/l, $P = 0.035$).

Figure 1 demonstrates stratified analysis to illustrate the modifying effects of BMI on the association between amounts of SSB consumption and CRP concentrations because BMI has been suggested to be an important modifier in inflammation. In this study, BMI status may modify the association between amount of SSB intake and inflammation after performing multivariate regression model with interaction term (P for interaction term was 0.035). Stratified analysis was further performed to examine whether there were different associations between SSB consumption and inflammation among adults who were overweight and obesity. No associations between amount of SSB intake and CRP level were found in adults with

normal weight or overweight ($P = 0.548$ and 0.311). However, obesity may have affected the association between amount of SSB intake and CRP levels. Obese adults who were medium (351–699 ml/day) and heavy SSB consumers (≥ 700 ml/day) were both found to have significantly increased CRP levels than obese non-SSB consumers (aDiff. = 0.58 mg/l in medium and 0.50 mg/l in heavy SSB consumers, respectively; $P = 0.014$ and 0.013).

Discussion

Findings from this study show that adults who consume the highest amounts of SSB (≥ 700 ml/day) possessed higher CRP levels than non-SSB consumers, after controlling for potential confounders. This relationship was also shown to be modified by BMI status. After stratifying BMI status, obese adults who consumed medium and heavy amounts of SSB had significantly higher CRP levels.

Prior research in US adults has also demonstrated that elevated CRP levels are associated with an increased amount of SSB intake, after adjusting for demographic factors and socioeconomic status (Hert et al. 2014). However, in previous studies, relationships did not remain significant after controlling for BMI, substance use, total energy intake, and personal health conditions (Hert et al. 2014). Similar findings were noted in two additional studies on US and Mexican females (Tamez et al. 2018; Yu et al. 2018), and added sugar intake in the form of beverages was shown to increase inflammatory outcomes in another randomized control study (Aeberli et al. 2011). A limitation of these studies is that most focused on specific populations, such as in only men (Aeberli et al. 2011; de Koning et al. 2012), only women (Tamez et al. 2018; Yu et al. 2018), and/or pediatric populations (Kosova et al. 2013). Furthermore, inconsistent methodologies were used across studies, including varied definitions of SSB intake by frequency (de Koning et al. 2012; Tamez et al. 2018; Yu et al. 2018) or quantity of sugary drink intake. In addition, adjusted results of former studies differed (e.g., total energy intake (de Koning et al. 2012; Tamez et al. 2018); BMI status (Kosova et al. 2013; Tamez et al. 2018)), and one study defined “added sugar intake” to include fructose and glucose (Della Corte et al. 2018).

To address these inconsistencies in prior research, we used NHANES data to select study subjects who were 20 years old or above in our analyses. In addition, all types of sweetened drinks with added sugar were carefully aggregated based on USDA codes. After controlling for potential confounders in the final model (e.g., age, gender, race, PIR, smoking and alcohol status, physical activity, disease history, total energy intake, and BMI), the present study found that heavy SSB (≥ 700 ml/day) consumption

Table 1 Distribution of C-reactive protein (CRP) levels by personal characteristics, lifestyle patterns, sugar-sweetened beverage (SSB) consumption, and body mass index (BMI) status in US adults based on the 2007–2010 National Health and Nutrition Examination Survey (NHANES)

	N* of subject	% ^a	Average of CRP (mg/l)		
			Mean ^a	SE ^a	P value
Total population	6856		2.2	0.04	
Demographic factors					
Age, years					< 0.001
20–34	1882	30.7	2.0	0.06	
35–49	1923	31.0	2.1	0.08	
50–64	1576	24.0	2.3	0.08	
65–80	1475	14.4	2.5	0.09	
Sex					< 0.001
Male	3498	50.5	2.0	0.05	
Female	3358	49.5	2.4	0.05	
Ethnicity					0.004
Non-Hispanic white	3620	74.8	2.1	0.06	
Non-Hispanic black	1200	10.5	2.5	0.09	
Other ^b	2036	14.8	2.3	0.07	
PIR group					< 0.001
Below poverty	1291	14.7	2.5	0.10	
100–199%	1668	19.5	2.4	0.08	
200–299%	996	15.1	2.2	0.07	
300–399%	670	12.7	2.0	0.14	
≥ 400%	1621	38.1	2.0	0.07	
Lifestyle patterns					
Cigarette smoking					0.010
Non-smokers	3694	54.3	2.1	0.05	
Former smokers	1571	22.9	2.2	0.09	
Current smokers	1590	22.8	2.4	0.10	
Alcohol drinking					0.067
Nondrinkers	1829	22.1	2.4	0.07	
Light drinkers	3965	63.1	2.1	0.04	
Heavy drinkers	1062	14.9	2.3	0.08	
Physical activity					< 0.001
Low	4705	63.9	2.4	0.05	
High	2149	36.1	1.8	0.04	
Diseases ^c					< 0.001
No	4090	62.5	2.0	0.05	
Yes	2766	37.5	2.4	0.04	
SSB intake (ml/day)					0.047
Non-intake	1511	23.5	2.1	0.06	
< 350	1983	27.7	2.1	0.07	
351–699	1550	22.1	2.2	0.05	
≥ 700	1812	26.6	2.3	0.07	
BMI (kg/m ²)					< 0.001
Normal weight	2250	35.3	1.4	0.03	
Overweight	2544	36.2	2.1	0.06	
Obese	2062	28.6	3.3	0.06	

SSB, sugar-sweetened beverages; PIR, poverty income ratio; BMI, body mass index

*The raw number was not adjusted for sample survey design

^aThe results were adjusted for sampling weight^bEthnicity in the “other” group was a combination of Mexican–American and other Hispanic^cTypes of diseases included asthma, chronic bronchitis, emphysema, heart diseases, gout, arthritis, stroke, coronary heart disease (CHD), angina, heart failure, heart attack, anemia, any liver conditions, thyroid problems, and multiple types of cancer

Table 2 Effects of subjects' sugar-sweetened beverage (SSB) intake on C-reactive protein (CRP) levels after adjusting for potential confounders in US adults based on the 2007–2010 National Health and Nutrition Examination Survey (NHANES)

	Model 1 (univariate)			Model 2 (adjusted for demographic and lifestyle patterns)			Model 3 (adjusted for covariates in Model 2 and BMI)		
	Diff.	SE	<i>P</i> value	aDiff.	SE	<i>P</i> value	aDiff.	SE	<i>P</i> value
SSB intake (ml/day)									
Non-SSB drinkers	Ref.			Ref.			Ref.		
1–350	0.05	0.07	0.459	0.05	0.08	0.499	0.10	0.09	0.256
351–699	0.08	0.08	0.344	0.09	0.09	0.318	0.13	0.10	0.188
≥ 700	0.19	0.08	0.020	0.31	0.12	0.013	0.26	0.10	0.016
Demographic factors									
Age, years									
20–34	Ref.			Ref.			Ref.		
35–49	0.13	0.09	0.133	0.07	0.09	0.453	– 0.03	0.08	0.734
50–64	0.28	0.11	0.016	0.32	0.14	0.028	0.18	0.12	0.143
65–80	0.48	0.09	< 0.001	0.42	0.13	0.003	0.36	0.12	0.004
Gender (Ref = male)	0.43	0.07	< 0.001	0.35	0.08	< 0.001	0.55	0.07	< 0.001
Ethnicity									
Non-Hispanic white	Ref.			Ref.			Ref.		
Non-Hispanic black	0.41	0.12	0.001	0.36	0.12	0.005	0.15	0.10	0.148
Other ^a	0.24	0.10	0.018	0.23	0.10	0.031	0.07	0.10	0.455
PIR									
Below poverty	Ref.			Ref.			Ref.		
100–199%	– 0.04	0.10	0.679	0.02	0.11	0.866	0.01	0.09	0.889
200–299%	– 0.26	0.10	0.020	– 0.18	0.11	0.125	– 0.17	0.10	0.107
300–399%	– 0.36	0.13	0.011	– 0.33	0.17	0.057	– 0.26	0.14	0.078
≥ 400%	– 0.43	0.11	0.001	– 0.20	0.11	0.070	– 0.17	0.11	0.134
Cigarette smoking									
Non-smokers and former smokers	Ref.			Ref.			Ref.		
Current smokers	0.29	0.11	0.017	0.16	0.13	0.223	0.37	0.12	0.005
Alcohol drinking									
Nondrinkers and light drinkers	Ref.			Ref.			Ref.		
Heavy drinkers ^b	0.18	0.08	0.024	0.29	0.08	< 0.001	0.24	0.07	0.001
Physical activity (Ref = low) ^c	– 0.63	0.06	< 0.001	– 0.46	0.07	< 0.001	– 0.26	0.08	0.002
Diseases (Ref = no) ^d	0.37	0.05	< 0.001	0.25	0.07	0.001	0.09	0.06	0.141
Total energy intake (100 kcal/day)	– 0.2	0.004	< 0.001	– 0.01	0.006	0.134	– 0.01	0.005	0.056
BMI (kg/m ²)									
Normal weight	Ref.			Ref.			Ref.		
Overweight	0.66	0.06	< 0.001	–	–	–	0.77	0.07	< 0.001
Obese	1.85	0.07	< 0.001	–	–	–	1.92	0.07	< 0.001

SSB, sugar-sweetened beverages; BMI, body mass index; aDiff., adjusted difference; Ref., reference group; PIR, poverty–income ratio

*An interacting effect was detected in medium SSB consumers with obesity in the full model ($P = 0.035$)

^aEthnicity in the “other” group was a combination of Mexican–American and other Hispanic

^bAlcohol drinkers who had 5 or more drinks in a single day during the past 12 months were defined as heavy alcohol drinkers

^cParticipants with ≤ 1200 MET-mins/week were defined as having low physical activity

^dTypes of diseases included asthma, chronic bronchitis, emphysema, heart diseases, gout, arthritis, stroke, CHD, angina, heart failure, heart attack, anemia, any liver conditions, thyroid problems, and multiple types of cancer

was associated with a 0.26 mg/l average increase in CRP level when compared to non-SSB drinkers ($P = 0.016$). Moreover, obesity level modified this relationship, which

supports prior research demonstrating that BMI strongly confounds the association between SSB consumption and inflammation (Schulze et al. 2005; Tamez et al. 2018).

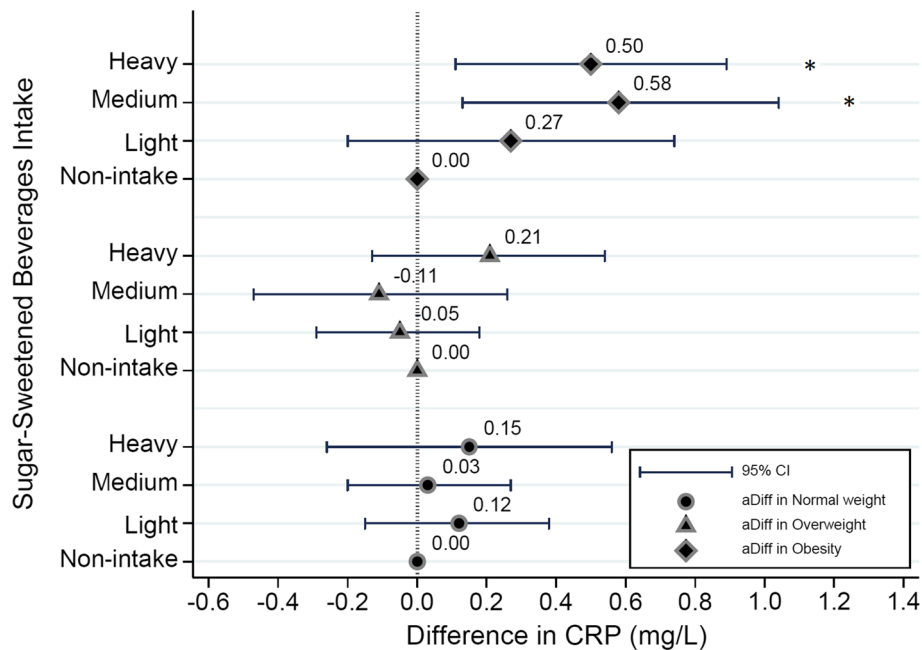


Fig. 1 Different effects of sugar-sweetened beverages (SSB) intake on C-reactive protein (CRP) levels among body mass index (BMI)-stratified SSB consumers based on the 2007–2010 National Health and Nutrition Examination Survey (NHANES) data. The multivariate-adjusted differences were estimated under a linear regression model adjusted for the age, gender, race, poverty–income ratio (PIR), cigarette smoking and alcohol drinking, total calories intake, diseases,

and physical activity. SSB, sugar-sweetened beverages; CRP, C-reactive protein; non-intake, non-SSB drinkers; light, 1–350 ml/day; medium, 351–699 ml/day; heavy, ≥ 700 ml/day. *Significant difference in CRP ($P = 0.014$ and 0.013) was estimated among medium and heavy SSB consumers compared to non-SSB consumers within obese group

Our study further evaluated the interacting effect of amount of sugary drinks and BMI on CRP level ($P = 0.035$). BMI status may also be a modifier that affects the association between amount of SSB intake and CRP level in our current findings. After stratifying BMI status, no association was found between the amount of SSB intake and CRP level in normal weight and overweight participants. Findings show that obese adults who consumed medium (350–699 ml/day) and heavy (≥ 700 ml/day) amounts of SSB had a 0.58 and 0.50 mg/l higher CRP level than obese non-SSB drinkers, respectively. It is well documented that adults with obesity have increased levels of circulating pro-inflammatory cytokines compared to non-obese individuals (Asghar and Sheikh 2017). Specifically, increased adiposity and metabolic syndrome have been associated with low-grade inflammation (Rodriguez-Hernandez et al. 2013). One previously identified source of these inflammatory markers is accumulated adiposity, in particularly visceral adipose tissue (VAT) (Unamuno et al. 2018). Pro-inflammatory adipokines, such as CRP, are deleterious and lead to adverse cellular consequences (Asghar and Sheikh 2017; Unamuno et al. 2018). Additionally, in adults, increased VAT is followed by macrophage infiltration leading to a state of chronic low-grade inflammation (Asghar and Sheikh 2017; Hotamisligil and Erbay 2008; Weisberg et al. 2003). This

sequence of events has led researchers to identify obesity as an inflammatory condition (Asghar and Sheikh 2017; Fernandez-Real et al. 1998; Unamuno et al. 2018), which is associated with increased production of cytokines such as interleukin (IL)-1, IL-6, IL-8, tumor necrosis factor α (TNF- α), and CRP, among others. Another important factor is leptin, which is expressed in adipose tissue, to affect pro-inflammatory and promotes obesity-related inflammation (Hauner 2005). One recent epidemiological research demonstrated that soda, but not diet soda, is directly associated with increased levels of CRP and leptin (Tamez et al. 2018). However, this study focused on the effect of soda intake in women only by using food frequency questionnaire (FFQ), and they did not demonstrate whether the observed effects varied by BMI status. Our study provides novel findings of an increased risk of elevated inflammatory state among individuals who consume more than one can of soda per day.

Consistent with prior evidence, we found that adults who were above 50 years old, female, black, of lower PIR, reported low physical activity, current smokers, and possessed medical conditions had higher CRP levels. Aging has been well understood as an important risk factor for developing aged-related chronic disease and increased inflammatory biomarkers (Singh and Newman 2011). In addition, different distributions of body fat between genders

may be a critical contributor to varying CRP levels between genders (Khera et al. 2009). Moreover, blacks have generally been observed to have higher inflammatory biomarkers than whites. However, the effect of ethnicity on inflammation might be better explained by lifestyle patterns and health-related conditions (Alley et al. 2006; Paalani et al. 2011). Cigarette smoking has been strongly linked to a higher CRP (O'Connor and Irwin 2010). Additionally, increased socioeconomic status and adequate physical activity have been demonstrated to lower inflammatory biomarkers (Alley et al. 2006; O'Connor and Irwin 2010). To evaluate the robust association between SSB consumption, BMI status, and CRP, most of these suggested potential confounders were controlled for in this study.

Limitation and strengths

Some limitations in this study should be noted. First, cross-sectional survey data cannot infer a causal relationship between SSB intake, BMI, and inflammation. Second, over-reporting or underreporting might have occurred during the 24-h dietary recall interview, but this bias due to misclassification would increase the likelihood of a null result. This study did not use other measurement tools, such as the Statistical Program to Assess Dietary Exposure (SPADE), to calculate a long-term habitual intake distribution (Dekkers et al. 2014; Dodd et al. 2006). The 24-h recall interviews may not reflect long-term habitual dietary intake patterns. In this study, we focused on SSB intake as a singular dietary variable. Therefore, we carefully identified each SSB intake and calculated the total amount of SSB intake based on suggested USDA codes that were transformed by NHANES staffs. This method should lower the bias of SSB intake estimation while using NHANES data. Third, data on personal health conditions may be underestimated because participants may not have yet been diagnosed with diseases, or did want to disclose their medical condition(s). Fourth, because blood specimens were collected after the questionnaire interviews, underreporting of SSB intake is unlikely to have occurred due to participants' knowledge of their clinical examinations.

Despite these limitations, this study has several strengths. First, our findings support the association between the amount of SSB intake, CRP level, and being overweight/obese, even after controlling for potential confounders. Secondly, in contrast to the previous research that only considered BMI as a confounder or did not control for BMI, our study explicitly evaluated how BMI modified the association between SSB intake and inflammation after adjusting for other potential confounders. In addition, we carefully identified and calculated each type of sweetened drink using food codes from the USDA. Dietary information in this study was also considered, in

order to calculate average total energy intake and SSB consumption. Lastly, we utilized NHANES data, a nationally representative survey of the US population.

Conclusions

In conclusion, excessive consumption of SSB is associated with elevated CRP in US adults, after controlling for potential confounders. However, BMI modifies this positive association between SSB consumption and CRP levels. Individuals with obesity who consume medium and heavy amounts of SSB may have increased cardio-metabolic disease risk via an enhanced inflammatory profile and therefore should be targets for future efforts to reduce SSB consumption.

Compliance with ethical standards

Conflict of interest The authors declare no conflict of interest.

Research involving human participants and/or animals This research was conducted using the National Health and Nutrition Examination Survey (NHANES) data. NHANES is a program of studies designed to assess the health and nutritional status of adults and children in the USA.

Informed consent This study was conducted using the National Health and Nutrition Examination Survey (NHANES) data. The research protocol was reviewed and approved by the Institutional Review Board at the National Center for Health Statistics before conducted data collection. Informed consent was signed from each study participant.

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