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RESEARCH ARTICLE

Sugary beverages are associated with cardiovascular risk factors in diabetic patients

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Abstract

Purpose Sugar-sweetened beverages (SSBs) containing high amount of added sugars have increased over the last decades. Due to increased risk of cardiovascular events in type 2 diabetes mellitus (T2DM) patients, we designed a study to assess the association between SSBs and metabolic syndrome, a collection of cardiovascular risk factors, in these patients.

Methods A cross-sectional study was performed on T2DM adults ($N = 157$). Participants had no serious disease or insulin treatment. SSBs records were obtained from a validated food frequency questionnaire. Metabolic syndrome status was extracted from biochemical and anthropometric measurements. Subjects risk factors were compared based on their usual SSBs consumption.

Results About half of participants consumed at least one serving of SSBs (Mean intake: 145.6 mL/d) on a weekly basis. Men and women had a similar SSBs pattern. Demographic and anthropometric characteristics were identical in both groups. Higher SSBs intake (≥ 0.5 vs <0.5 serving/ week) was positively associated with hypertension (OR: 3.48, 95% CI: 1.31, 9.26) and obesity (OR: 4.61, 95% CI: 1.31, 16.25). After adjustment for confounders, a higher risk of the metabolic syndrome was observed in those with higher SSBs intake (OR: 4.23, 95% CI: 1.42, 12.62).

Conclusion Drinking SSBs, even in low amounts, could potentially elevate the risk of cardiovascular risk factors in diabetic patients. Reduction of sugary drinks would be an urgent recommendation.

Keywords Diabetes · Metabolic syndrome · Sugar-sweetened beverages · Cardiovascular risk

Introduction

Diabetes is a chronic endocrine situation affecting about 415 million people worldwide and over 4.6 million cases in Iran (http://www.idf.org/membership/mena/iran I). It puts a huge burden on health systems and governments and its annual economic health expenditure is estimated at 673 billion dollars. We will witness a surge in diabetes cases by 2040 and the highest elevation is expected for the Middle East and North Africa by up to 103.8% [1]. Cardiovascular disease (CVD) [2] is a major consequence of diabetes and contributes to about one-third of total mortalities in this population [3]. A collection of metabolic abnormalities, namely metabolic syndrome (MetS), can potentially predict the risk of future CVD events [4] while diabetes itself is a component of MetS [4].

Beverages, mainly sugar-sweetened beverages (SSBs), as a part of diet involve in diabetes management [5–8]. Some surveys claimed that sugary beverages contribute to obesity and CVD. They are also supposed to increase insulin resistance, inflammation [9], hypertension [10], adiposity [11, 12], and lipogenesis [13, 14]. The Framingham Offspring Study demonstrated increased incidence of hypertension after four years consumption of ≥1 serving soft drink/day by 22% [15] and also higher incidences of hypertriglyceridemia and low level of high-density lipoprotein cholesterol (HDL-C) compared with non-consumers [15]. Also, the Nurses' Health Studies I and II revealed that women who had consumed ≥4 serving SSBs in a day had 44% and 28% elevated risk of incident

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hypertension [16]. According to the Multi-Ethnic Study of Atherosclerosis (MESA) findings, daily SSBs consumption resulted in hypertriglyceridemia, hypertension and low levels of HDL-C [17]. Cross-sectional analysis of NHANES data found a positive association between SSBs intake and blood pressure in adolescents [18]. An interventional study suggested that markers of inflammation, including serum haptoglobin, transferrin, and C-reactive protein, increase following sucrose intake [19]. Indirect evidence from observational studies has found positive associations between dietary patterns that are high in SSBs with markers of inflammation such as C-reactive protein and tumor necrosis factor receptor-2 [20] and dietary glycemic load, to which SSB intake was a large contributor to C-reactive protein [21].

Global intake of SSBs is 0.58 serving/day [22] while in a national report, the mean daily SSBs consumption in Iranians is 48.9 ± 77.8 g [23]. National Health and Nutrition Examination Survey (NHANES 2003–2006) determined that 45% of T2DM adults were SSBs consumers [2], but no report is available regarding the current intake in Iranian diabetes afflicts. International federations, such as the American Cancer Society, the American Diabetes Association, and the American Heart Association propose rigorous constraint of sugar-added beverages in people with diabetes [24]. On the other hand, according to a national investigation, one-third of Iranian adults have MetS [25] while the rate is extremely higher in type 2 diabetes mellitus (T2DM) patients by up to 84.1% of the population [26] which warns us about considerable cardiovascular outcomes in near future.

Regarding the elevated MetS rate observed in national investigations in diabetic people and due to an increased mortality from CVD in these patients and its huge health burden, we performed a study to evaluate the association between SSBs intake and cardiovascular risk predictors in these patients.

Materials & methods

Ethics

The study complied with the Declaration of Helsinki and Ahvaz Jundishapur University of Medical Sciences Research Ethics Committee approved the protocol (Medical ethics code no. IR.AJUMS.REC.1394.55). Volunteers declared their consent through a written form and were informed about the study at the beginning.

Subjects

T2DM adult outpatients aged ≥20 years old referred to Diabetes Clinic of Golestan Hospital in Ahvaz were recruited for the study. A general practitioner confirmed their diabetes according to the American Diabetes Association (ADA) criteria [27]. Subjects with insulin therapy, being under special diet treatment during the previous three months or having any serious disease, like cancers, kidney failures, heart attack, etc., were excluded from the primary sample. Some patients did not attend to blood sampling. The final sample included 157 patients.

Personal data Demographic data including age, sex, smoking status, and physical activity level were recorded through face to face interview. Drugs history, including oral hypoglycemic agents (OHAs), lipid-lowering drugs, and anti-hypertension treatment, was taken from each participant. A trained dietician measured weights (kg) and body fat (%) using a standard digital scale to the nearest 100 g (Omron 212, Omron Corporation, Germany) in subjects with light clothes without shoes. Heights (meter) were twice recorded to the nearest 0.5 cm in the upright position without shoes using a standard tape meter and finally, the mean values were considered. Afterward, body mass index (BMI) was calculated by dividing weight (kg) to squared height (m2). Waist circumference (WC) was measured using a flexible tape-meter to the nearest 0.5 cm. All the devices were calibrated at the day of examination. Physical activity was determined by completing the international physical activity questionnaire (short version) and it was converted into low, moderate, and high activity levels [28]. Blood pressures were measured by a registered nurse using standard protocols.

Biochemical assays Blood samples were drawn after at least 8 h of fasting. The blood samples located in a cool box were sent to the laboratory of Diabetes Research Center in Ahvaz Jundishapur University of Medical Sciences within an hour. Samples were centrifuged to collect serums. Standardized enzymatic colorimetric methods were performed to determine lipid profile, including cholesterol (Chol), high density lipoprotein cholesterol (HDL-C), low density lipoprotein cholesterol (LDL-C) and triglycerides (TG) (Pars Azmun kits, Pars Azmun Co., Karaj, Iran) using a calibrated auto-analyzer device (B.T. 3000, Biotecnica instruments, Italy). LDL-C levels were derived using Friedewald equation [29] and in case of high TG concentrations, LDL kit was used (Pars Azmun kits, Pars Azmun Co., Karaj, Iran).

Metabolic syndrome definition Abdominal obesity (WC ≥94 cm for men and WC ≥80 cm for women) plus at least two of the following metabolic abnormalities, according to the International Diabetes Federation criteria were considered as MetS [4]: 1. previously diagnosed diabetes [27] or high fasting blood glucose (≥100 mg/dL); 2. hypertriglyceridemia (TG ≥150 mg/dL or use of medication); 3. low HDL-C (HDL-C < 40 mg/dL for men and < 50 mg/dL for women); 4. elevated blood pressure (BP) (systolic BP ≥130 or diastolic BP ≥ 85 mmHg or use of medication).

Sugar-sweetened beverages SSBs consumption and other dietary habits were extracted from a 86-item validated food frequency questionnaire (FFQ) [26]. Sweetened beverages like syrups, soft drinks, commercial fruit juices, sweetened milk, sweetened tea or coffee, and other sugary drinks were recorded as 8-oz servings. Dietary energy and macronutrient contents were extracted from FFQs using Nutritionist-IV® software modified for Iranian food tables.

Statistical analysis Subjects were categorized into two groups according to their median SSBs intakes: <0.5 and ≥ 0.5 serving/week. Data were analyzed using SPSS software (IBM® SPSS Statistics Corporation, IL, USA, version 21.0). A significant difference was described as p values less than 0.05. Logistic regression, Chi-square test, Pearson's correlation, and independent t-test were used to demonstrate associations among variables. Odds ratios and confidence intervals were also reported.

Results

Primarily, 53 males and 104 females entered the study. Mean age of participants was 54.5 year (Minimum: 29.0, Maximum: 75.0). The average daily intake of SSBs was 0.6 serving or 145.6 mL. Less than half of participants consumed at least 1 serving of SSBs a day (45.2%). Of participants, 77 patients consumed less than 0.5 (49%) and 80 cases had ≥0.5 serving SSBs per week (51%). Totally, 87.9% of patients were abdominally obese, 75.8% had hypertension, 43.3% had hypertriglyceridemia, and 63.1% had low HDL concentrations.

Comparison of basic characteristics based on SSBs intake is depicted in Table 1. The similar distributions of genders were seen in two SSBs groups. Also, the age, anthropometric measures (WC, BMI) and physical activity were similar in both categories. No association was observed between diabetes duration and SSBs groups (Table 1). Although dietary energy and the proportion of fat were alike, subjects consuming higher sugary drinks had higher carbohydrate (OR: 1.04, $p = 0.05$, Table 1) and lower protein intake (OR: 0.83, $p = 0.02$, Table 1). There was no difference between FBS, TG, cholesterol, HDL-C and LDL-C levels between the two SSBs groups (Table 1).

Similar values were found for systolic blood pressure in both groups but mean diastolic blood pressure was higher in group 2 (≥0.5 serving SSBs /week) (84.96 vs. 81.74 mmHg; OR: 1.03, 95% CI: -6.54, 0.10; $p = 0.06$). Drugs history, including oral hypoglycemic agents (OHAs), lipid-lowering drugs, and anti-hypertension treatment, was compared using Pearson Chi-square in the abovementioned groups and as seen in Table 1 the differences were not considerable.

Participants consuming 0.5 serving SSBs/week or more had 4.18 (95% CI: 1.19, 14.67), 4.24 (95% CI: 1.26, 14.25), and 3.64 times (95% CI: 1.01, 13.21) higher risk of having 3, 4 and 5 metabolic risk factors, respectively (after adjustment for age, sex, educational level, and physical activity). The results remained significant even after additional adjustment for BMI and energy (Table 2). Although more SSBs intake was associated with higher number of metabolic abnormalities (P for trend = 0.039), further adjustment for BMI and energy attenuated the association ($P = 0.063$; Table 2).

As observed in Table 3, rather high prevalence of elevated blood pressure, obesity, impaired HDL and increased FBS concentrations were seen in both groups (Table 3). The group with higher SSBs consumption (≥0.5 serving /week) had higher rates of hypertension (OR: 3.48, 95% CI: 1.31, 9.26; Table 3). Although BMI showed no correlation with SSBs intake, ≥0.5 serving SSBs/week had considerably elevated the risk of abdominal obesity (OR: 4.61, 95% CI: 1.31, 16.25). Patients who consumed ≥0.5 SSBs/week had 4.23 times higher risk of MetS after adjusting for confounders including age, sex, educational level, physical activity, and drug therapy (92.50% vs. 75.32%, 95% CI: 1.42, 12.62, $p = 0.01$, Table 3).

Discussion

The surprising rate of metabolic disorders in T2DM population warns health authorities to expect a huge burden of cardiovascular outcomes in upcoming years [26]. The growing global prevalence of T2DM along with the double risk of CVD in diabetic patients intensify the importance of controlling the underlying factors [30]. Increasing body of evidence suggests the contributing role of SSBs in coronary heart disease (CHD). After a 24-year follow-up of the Nurses' Health Study, 35% greater risk of developing CHD was observed in women consuming 2 SSBs/day rather than <1 SSB/month which remained statistically significant even after adjustment for BMI and energy intake [7].

The present study demonstrated that 45% of T2DM participants consumed SSBs that was in accordance with Bleich et al. findings from NHANES [2]. In our study one-fifth of subjects consumed at least 1 serving of SSBs a day which is noteworthy. Also, we noticed that higher SSBs intake is accompanied by greater proportion of energy from carbohydrate and lower proportion from protein, which is in consistence with a recent study in healthy Iranian adults [31].

From one point of view, SSBs may result in adipose tissue accumulation [11, 12]. Abdominal obesity, as a prevalent MetS component in diabetic patients [8, 32], is supposed to have a strong association with CVD and death [33, 34]. The present study suggests that drinking 0.5 or more servings of SSBs in a week is associated with 4.6 fold greater odds of abdominal obesity. Lipid accumulation can induce inflammatory cytokines release from macrophages [35]. Adiposity increases

Table 1 Participants' baseline characteristics

Variable	SSBs intake				
	Group1 (N = 77)	Group2 (N = 80)	OR	95% CI	*p* value
Demographic data					
Sex (%)					0.50
Male	36.36	31.25	1.00		
Female	63.64	68.75	1.26	0.65, 2.44	
Age (%)					0.54
< 50 year	28.57	35.00	1.00		
50–55	15.58	20.00	1.05	0.41, 2.67	0.92
55–60	18.18	17.50	0.79	0.31, 1.99	0.61
≥ 60	37.66	27.50	0.60	0.27, 1.31	0.20
Diabetes duration (%)					0.35
< 5 year	63.636	56.25	1.00		
≥ 5 year	36.363	43.75	1.36	0.72, 2.58	
Physical activity (%)					0.76
High	7.79	7.50	1.00		
Moderate	46.75	41.25	0.92	0.27, 3.12	0.89
Low	45.45	51.25	1.17	0.35, 3.96	0.80
Education Level (%)					0.05
higher education	5.26	6.25	1.00		
diploma	22.37	30.00	1.13	0.26, 4.84	0.87
undergraduate	56.58	35.00	0.52	0.13, 2.11	0.36
illiterate	15.79	28.75	1.53	0.35, 6.79	0.57
Smoking status (%)					0.30
Current	2.60	6.25	1.00		
Former	6.49	11.25	0.72	0.10, 5.17	0.74
Never	90.90	82.50	0.38	0.07, 2.01	0.25
Anthropometric data					
BMI (kg/m^2)	28.65 ± 5.26	29.84 ± 4.77	1.05	0.99, 1.12	0.14
Waist circumference(cm)	97.36 ± 10.78	99.57 ± 9.55	1.02	0.99, 1.05	0.18
Biochemical data					
FBS (mg/dL)	164.61 ± 86.07	150.73 ± 54.95	0.24	−8.79, 36.56	0.23
TG (mg/dL)	147.48 ± 84.95	164.19 ± 88.36	0.24	−44.05, 10.64	0.23
Chol (mg/dL)	168.13 ± 40.22	176.35 ± 37.24	0.19	−20.43, 3.99	0.19
HDL(mg/dL)	43.81 ± 9.37	44.40 ± 10.18	0.70	−3.68, 2.49	0.70
LDL(mg/dL)	95.22 ± 30.55	100.71 ± 31.01	0.27	−15.19, 4.22	0.27
Blood pressures					
Systolic (mmHg)	127.73 ± 18.15	132.79 ± 19.47	1.02	−11.00, 0.80	0.09
Diastolic(mmHg)	81.74 ± 9.85	84.96 ± 11.14	1.03	−6.54, 0.10	0.06
Blood pressures					
Systolic (mmHg)	127.73 ± 18.15	132.79 ± 19.47	1.02	−11.00, 0.80	0.09
Diastolic(mmHg)	81.74 ± 9.85	84.96 ± 11.14	1.03	−6.54, 0.10	0.06
Dietary data					
Energy (kcal/kg/d)	34.81 ± 1.28	34.29 ± 1.28	1.00	0.97, 1.02	0.77
Carbohydrate (gr/day)	56.60 ± 1.16	59.36 ± 0.81	1.04	1.00, 1.08	0.05
Protein (gr/day)	13.75 ± 0.27	12.93 ± 0.22	0.83	0.71, 0.97	0.02*
Fat (gr/day)	29.49 ± 1.16	27.55 ± 0.83	0.98	0.94, 1.01	0.17
Medication history					
OHA (%)	94.81	88.75	0.91	0.74, 1.13	0.07
HLP medication (%)	54.55	53.75	0.97	0.52, 1.82	0.92
HTN medication (%)	49.35	52.50	1.13	0.61, 2.12	0.69

Values are presented as Mean ± SD or percentage. * $P < 0.05$ is significant

Group 1: <0.5 serving SSBs per week; *Group 2:* ≥0.5 serving SSBs per week

Chol, cholesterol**;** *FBS,* fasting blood sugar; *HDL***,** high-density lipoprotein**;** *HLP*, hyperlipidemia; *HTN*, hypertension; *LDL*, low-density lipoprotein**;** *OHA,* oral hypoglycemic agents; *SSBs*, sugar-sweetened –beverages; *TG*, Triglyceride

Table 2 Cardiovascular risk factors association with sugary beverages consumption

Number of risk factors	N (%)	SSBs (serving/wk) [#]	Group 1 (N = 77) (%)	Group 2 (N = 80) (%)	Crude OR (95%CI)	OR[a] (95%CI)	OR[b] (95%CI)
0–2	25 (15.9)	2.06 ± 0.86	24.68	7.50	1.00	1.00	1.00
3	39 (24.8)	4.09 ± 1.00	22.08	27.50	4.10* (1.34, 12.50)	4.37* (1.30, 14.65)	4.18* (1.19, 14.67)
4	56 (35.7)	5.39 ± 1.10	31.17	40.00	4.22* (1.46, 12.18)	4.42* (1.36, 14.31)	4.24* (1.26, 14.25)
5	37 (23.6)	4.18 ± 1.30	22.08	25.00	3.73* (1.21, 11.45)	3.84* (1.13, 13.09)	3.64* (1.01, 13.21)
Total	157 (100)	4.25 ± 0.57	100.00	100.00	$P = 0.012$*	$P = 0.039$*	$P = 0.063$

Group 1: <0.5 serving SSBs per week

Group 2: ≥0.5 serving SSBs per week

SSB, sugar sweetened beverage

[#] Mean ± SEM. Chi-square and logistic regression analyses were used

*$P < 0.05$ is significant

[a] Model 1: Adjusted for age, sex, educational level, physical activity

[b] Model 2: Adjusted for BMI, energy, age, sex, educational level, and physical activity

serum concentrations of leptin and leads to leptin resistance in obese subjects [36] which has inflammatory effects [37].

Furthermore, recent studies demonstrated that about half of diabetic population has hypertension [8, 38]. A meta-analysis of randomized control trials also concluded that diets with high sugar content compared to low-sugar ones result in increased blood pressure [39]. Considering the fact that hypertension is a potent CVD risk factor and regarding our findings, we support the mediating effect of SSBs in CVD through that. Sugar-induced leptin resistance may contribute to blood pressure

Table 3 Prevalence of metabolic disorders according to SSBs intake

Metabolic disorder	SSBs category		Crude OR (95% CI)	OR(95% CI) [#]	*P* value [#]
	<0.5 serving/week (*N* = 77)	≥0.5 serving/week (*N* = 80)			
Hypertension (%)					0.01*
Yes	67.53	83.75	2.48 (1.16–5.31) *	3.48 (1.31, 9.26)	
No	32.47	16.25	1.00	1.00	
Abdominal Obesity (%)					0.02*
Yes	80.52	95.0	4.60 (1.45–14.56) *	4.61(1.31, 16.25)	
No	19.48	5.00	1.00	1.00	
Hypertriglyceridemia (%)					0.79
Yes	41.56	45.00	1.15 (0.61–2.17)	1.09 (0.57, 2.11)	
No	58.44	55.00		1.00	
Low HDL (%)					0.14
Yes	66.23	60.00	0.77 (0.40–1.47)	0.59 (0.29, 1.19)	
No	33.77	40.00	1.00	1.00	
Impaired FBS (%)					0.30
Yes	89.61	83.75	0.60 (0.23–1.53)	0.59 (0.22, 1.59)	
No	10.39	16.25	1.00	1.00	
Metabolic syndrome (%)					0.01*
Yes	75.32	92.50	4.04 (1.52–10.77) *	4.23 (1.42, 12.62)	
No	24.68	7.50	1.00	1.00	

Chi-square and logistic regression analyses were used

CI, confidence interval; *FBS*, fasting blood sugar; *OR*, odds ratio; *SSB*, sugar sweetened beverages; *wk*, week

[#] Adjusted for age, sex, educational level, physical activity, and drug therapy

* $P < 0.05$ is significant

[40]. Dietary sugar can also increase blood pressure by activating the sympathetic nervous system, which stimulates angiotensin II and aldosterone production from adrenal glands [41].

SSBs is supposed to increase hepatic lipogenesis [13]. Although some cross-sectional studies in adults showed a significant correlation between caloric sweetener consumption and dyslipidemia [42], we did not find such association and it seems that further investigations in this case are required.

The Framingham Heart Study showed that consuming one serving of SSBs per day, independent of weight status, doubled the metabolic disorders, compared to non-consumers [43]. Based on our investigation, we also hypothesized that MetS is associated with SSBs. Some proposed mechanisms are obesity [44], high dietary glycemic load, insulin resistance, β-cell dysfunction, and inflammation [9]. The high content of rapidly absorbed carbohydrates such as sucrose and high-fructose corn syrup in SSBs, in conjunction with the large volume consumed, also may lead to hypertension [10], visceral and ectopic adipose tissue accumulation [11, 12], and hepatic lipogenesis elevation [13]. Increased uric acid production and lower levels of the vasodilator Nitric Oxide resulted from sugar are other possible factors [45, 46]. Other plausible mechanisms are decreased sodium excretion, increased sodium absorption in the gut and activation of the sympathetic nervous system [46, 47].

Limited investigations have related SSBs to cardiovascular hazard, however, accumulating evidence proposes SSBs' role in the development of hypertension, lipid abnormality, inflammation, and coronary heart disease (CHD). Our study supports this fact that SSBs intake is associate with increased odds of MetS in T2DM, however, some limitations confine the generalization of the results. First, its cross-sectional design hinders drawing a cause-effect relationship between SSB and MetS. Second, recall bias may potentially influence the results. Third, FFQs could result in underreporting and misclassification of exposure. And the last issue, like any cross-sectional study, we could not demonstrate the direction of relationships between variables, and accordingly, modifying the long-standing dietary habits after diabetes diagnosis could be happened as a true event. This issue can be covered through longitudinal studies in the future.

Conclusion

To sum up, SSBs consumption in diabetic patients and its correlation with adverse metabolic outcomes necessitates considering practical strategies to decline the sugary beverages. However, long-term studies can better shed light on this association and distinguish any causal relationship. Until then, recommendation on lowering sugary beverages in these patients would be a reasonable practice.

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Compliance with ethical standards

Conflicts of interest The authors declare that they have no conflict of interest.

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