

Original Article

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The Association Between Healthy Beverage Index (HBI) With Metabolic Risk Factors Among Apparently Metabolically Healthy Overweight and Obese Individuals

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ABSTRACT

Recent studies have evaluated the association between specific beverage intake and metabolic risks in adults. However, more evidence is needed to examine the association between the Healthy Beverage Index (HBI) and metabolic factors. Therefore, this study investigated the relationship between HBI and metabolic factors in adults. In this cross-sectional study, 338 overweight and obese individuals living in Tabriz, Iran were selected. Data on beverage consumption, demographics, physical activity, and anthropometric characteristics were evaluated using validated standard protocols. The predefined HBI was calculated based on previous studies. The mean value of HBI index among all of the participants was 59.76 ± 6.51. Those at the higher HBI scores had significantly lower waist circumference, waist-tohip ratio, fat mass, and weight (p < 0.05). HBI and triglyceride scores also had a significant relationship. It has been shown that at higher HBI scores compared to lower scores, highdensity lipoprotein cholesterol levels increase while homeostatic model assessment for insulin resistance, low-density lipoprotein cholesterol, total cholesterol, and blood pressure decrease. HBI scores higher among Iranian adults were associated with a better chance of losing weight and weight loss and a better lipid profile, and lower blood pressure. Therefore, HBI can be a useful and helpful tool for assessing the overall quality of beverages adults consume. However, further studies are warranted to confirm the possible health effects of healthy beverage index.

Keywords: Healthy Beverage Index; Cardio-metabolic; Overweight; Obesity

INTRODUCTION

More than a third of adults worldwide are overweight (body mass index [BMI] of 25 to 29.9) and obese (BMI over 30) [1,2]. Obesity and overweight are among the most important

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Conflict of Interest

The authors declare that they have no competing interests.

Author Contributions

Conceptualization: Abbasalizad Farhangi M; Data curation: Tousi AZ, Nikrad N; Formal analysis: Jahanbazi L, Abbasalizad Farhangi M, Tousi AZ; Methodology: Jahanbazi L; Project administration: Abbasalizad Farhangi M; Supervision: Abbasalizad Farhangi M; Writing original draft: Abbasalizad Farhangi M; Writing - review & editing: Tousi AZ, Nikrad N. risk factors for mortality worldwide, causing various diseases such as type 2 diabetes, hypertension, cancer, and cardiovascular disease [3,4]. The prevalence of overweight in Iran is 42% in men and 57% in women, while 11.1% of men and 25.2% of women are obese [5].

The factors that predispose individuals to obesity include age, low physical activity, low level of education and awareness, living in urban areas, and following inappropriate eating diets such as high-calorie foods and drinks, including sugar-sweetened beverages (SSBs) [6]. A previous study showed that heredity and environmental factors could affect both the type and amount of beverage intake [7]. Water intake has important health benefits for the body [8]. Increasing water intake can be an important strategy for treating and preventing obesity [9,10]. Other beverages such as milk, tea, coffee, and other unsweetened beverages are also important for the health of the body [11,12]. Appropriate fluid consumption helps properly function the urogenital and gastrointestinal tracts [13,14] and thus reduces mortality [14,15]. SSBs cause weight gain and obesity, while decreased SSB intake reduces the risk of obesity and cardiovascular disease [16,17].

More attention is paid to receiving water than SSBs, recently [7,10]. Many studies have been conducted on the intake of SSBs and their association with obesity [18,19]. However, limited studies have examined the overall quality of daily beverages in a broader context [20,21]. Thus, a Healthy Beverage Index (HBI), like the Healthy Eating Index (HEI) [22], can be used to assess the overall quality of beverages received, as well as to determine whether improving the pattern of beverages consumed is associated with improved body health. Therefore, dietitians and therapists can use HBI as a counseling tool to promote healthy beverage choices.

One of the objectives of our study is to establish a scoring system to provide an indicator of the overall quality of beverages consumed, including determining the total index of liquids consumed, with the help of quantitative recommendations of beverages and liquids received [6,26, 27]. Another purpose of HBI is examining the relationship between HBI score, and metabolic outcomes in adults. Commonly consumed beverages in Iran are sweetened with sucrose, while in Western countries, beverages are sweetened with corn syrup high in fructose [28]. Therefore, the findings of Western studies cannot be generalized to other countries. Lastly, due to geographical diversity, our other goal was to assess the relationship between HBI and metabolic criteria in metabolically healthy overweight and obese adults in Tabriz, Iran.

MATERIALS AND METHODS

Participants

This cross-sectional study included 338 (total sample) overweight and obese people living in Tabriz, Iran. Participants in this study were selected by a combination of 2 projects [29,30] among overweight and obese individuals. Participants were collected through a call. Inclusion criteria were: age 20–70 years and BMI ≥ 25 kg/m². Exclusion criteria also included: pregnancy, lactation, menopause, bariatric surgery, cardiovascular disease, kidney disease, liver cancer, diabetes mellitus, and weight-bearing medications. Written consent approved by all participants was completed. Also, the study proposal was approved by the ethics committee of Tabriz University of Medical Sciences, Tabriz, Iran.

General characteristics and anthropometric assessments

Sociodemographic information such as gender, age, smoking rate, level of education,



marital status, occupation, and medical records was collected through a questionnaire. The socioeconomic status score was then obtained. Body composition measurements were also calculated by bioelectrical impedance analysis (BC-418 MA; Tanita, Tokyo, Japan).

The study samples were weighed with minimum clothing and without shoes using a Seca scale (Seca 755, seca GmbH, Hamburg, Germany) with an accuracy of 0.5 kg, which was controlled with a standard weight after every 10 times weighing the participants. Heights were measured with a plastic meter attached to the wall so that the participants stood on their feet without shoes while their knees, hips, shoulders, and back were along the plastic meter. The participants' heights were measured with an accuracy of 0.5 cm. The amount of physical activity was calculated using a short 7-item International Physical Activity Questionnaire [31]. The abbreviated version of this questionnaire includes seven simple questions (the validity and reliability of which have already been measured). Waist circumference with light clothing and in the distance between the smallest area under the ribs and above the iliac spine and hip circumference in the largest hip circumference was measured with the help of an inelastic tape meter without any pressure per meter with an accuracy of 0.1 cm. Waist-to-hip ratio (WHR) and BMI were also measured. Blood pressure was also measured using a standard mercury sphygmomanometer twice in one arm after at least 15 minutes of rest, then the average of two measurements was analyzed. Metabolic syndrome (MetS) was defined according to National Cholesterol Education Program Adult Treatment Panel III criteria [32].

Dietary assessment and definition of HBI

The 147-item food frequency questionnaire (FFQ) was used to measure food consumption; its validity and reliability were established in a previous study by Esfahani et al. [33]. Participants were asked to detail the types and quantities of all the foods they consumed over a year. Dietary intake information was recorded for each food items in a daily, weekly, and monthly manner. To determine the proportion of sugary drinks consumed in Iran among the total consumption of non-alcoholic beverages and industrial fruit juices, we divided weekly intake by 7 or monthly intake by 30 and then converted the result back to daily consumption [34].

Duffey and Davy's [35] approach was used to calculate the HBI. Consumed beverages were grouped into 8 categories, including water, unsweetened coffee or tea, low-fat milk (less than 1.5% fat, fat-free, and/or soy milk), diet drinks (including non-caloric sweetened coffee or tea and other artificially sweetened beverages), 100% natural fruit juice, alcohol (including beer, wine, and liquor), full-fat milk (1.5% fat), and sugar-sweetened beverages (including fruit drinks, sweetened coffee, tea, and soda) [35]. The final HBI score ranges between 0 and 100, with a higher value demonstrating better adherence to beverage guidelines and a healthier beverage intake pattern [35]. However, as in the current study, diet drinks (ranging from 0 to 5) and alcohol (ranging from 0 to 5) were not consumed by our target population, and the maximum final HBI score was 90. As the present study aimed to investigate adherence to healthy beverage intake guidelines and not total fluid consumption, liquids consumed as part of food (such as soup) were not included.

Biochemical assessment

Initially, after 10–12 hours of fasting, the laboratory technician took 10 mL of venous blood from all samples. Blood samples were then centrifuged for 10 minutes to separate serum and plasma. Lipid profiles, including triglycerides (TGs), total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), and insulin, were measured by special spectrophotometric and enzyme-linked immunosorbent assay kits. In addition, low-density lipoprotein



cholesterol (LDL-C) levels were estimated by the Friedwald equation [36]. The homeostatic model assessment for insulin resistance (HOMA-IR) was evaluated using the following formula: fasting insulin (μ IU/ml), fasting glucose (mmol/L)/22.5 and the quantitative insulinsensitivity check index as:

Log Insulin Fasting (μU/mL)+Glucose Log (mmol/L)

Statistical analyses

The statistical analysis of the data was performed using the statistical package for social sciences (SPSS) (version 21.0; IBM Corp., Armonk, NY, USA). The p values less than 0.05 were considered significant. The mean, standard deviation (SD) was used for reporting quantitative data. For qualitative data, the number and percentage (%) were used. Differences in discrete and continuous variables at different levels of HBI categories were compared using χ^2 and one-way analysis of variance tests, respectively. Analysis of covariance was used to compare biochemical variables after adjusting for confounding factors (age, sex, BMI, and physical activity).

Ethics statement

The ethics committee of the Tabriz University of Medical Sciences has approved this study protocol (code: IR.TBZMED.REC.1401.087 and grant number: 68837). Written informed consent was obtained from all participants before participating in the study. All methods in the current research were performed under the Declaration of Helsinki's guidelines and regulations.

RESULTS

Participants' general characteristics across HBI are shown in **Table 1**. There was a significant association between Kcal /day and HBI intake (p < 0.001). The results for other variables were not significant. **Table 1** also shows that at waist circumference (WC), WHR, fat mass (FM), and weight values decreased with HBI scores.

The energy-adjusted dietary intakes of participants in each tertile of HBI are shown in **Table 2**. All dietary intakes were significantly lower in higher tertiles of HBI (p < 0.05) except for vitamin K. However, after adjusting the confounders, many of these differences disappeared, and the intake of vitamin D, magnesium, and calcium decreased significantly across HBI tertiles in the adjusted model (p < 0.001).

The mean \pm SD of each of the 8 components of the HBI is presented for the full sample of adults as well as across tertile of HBI scores in **Table 3**. The average HBI score of Tabriz participants was 59.76 \pm 6.51. A difference of about 14 points separated the average HBI scores in the lowest and highest tertiles. The mean intake of water, coffee or tea, low-fat milk, 100% natural fruit juice, full-fat milk, and sugar-sweetened beverages did not differ across HBI tertiles (p > 0.05), whereas participants in higher HBI tertiles had higher intakes of total beverage energy and met total fluid requirements (p < 0.001).

The chemical properties of the participants are shown in **Table 4**. A significant relationship was found between HBI and TG scores. It has also been shown that at higher HBI scores (third tertile) than at lower scores (first tertile), HDL-C levels increase while HOMA-IR, LDL-C, TC, and blood pressure decrease (**Table 2**); meanwhile, these changes were not statistically meaningful (p > 0.05).



Characteristics	Tertiles of HBI					p value†
	1st (n = 112)	2nd (n = 113)	3rd (n = 113)	Total (n = 338)	_	
Sex					0.93	0.96
Male	77 (67.0%)	60 (52.2%)	65 (55.6%)	202 (58.2%)		
Female	38 (33.0%)	55 (47.8%)	52 (44.4%)	145 (41.8%)		
Education					0.64	0.65
Illiterate	1 (1.1%)	0 (0.0%)	1 (1.5%)	2 (2.6%)		
< 12 years	35 (58.3%)	35 (58.3%)	40 (58.8%)	110 (58.5%)		
≥ 12 years	24 (40.0%)	25 (41.6%)	27 (39.7%)	76 (40.4%)		
Occupation					0.75	0.93
No occupation	29 (48.4%)	35 (22.3%)	35 (51.5%)	99 (58.2%)		
Occupied	31 (51.7%)	25 (41.6%)	35 (48.5%)	91 (47.2%)		
BMI (kg/m²)	32.51 ± 4.71	33.05 ± 5.24	32.30 ± 4.45	32.62 ± 4.80	0.23	0.47
WC (cm)	107.53 ± 8.99	106.66 ± 10.26	106.17 ± 9.59	106.78 ± 9.62	0.27	0.55
WHR	0.94 ± 0.05	0.92 ± 0.08	0.93 ± 0.08	0.93 ± 0.07	0.14	0.15
FM (%)	32.43 ± 7.89	36.89 ± 11.21	32.30 ± 7.39	33.81 ± 9.13	< 0.001	0.06
FFM (%)	62.34 ± 11.73	62.37 ± 12.44	62.07 ± 12.97	62.25 ± 12.35	0.57	0.98
BMR	78.46 ± 15.94	79.45 ± 14.9	77.08 ± 17.76	78.34 ± 16.87	0.49	0.74
Total energy (kcal/day)	$3,426.14 \pm 344.30$	$2,806.0 \pm 351.5$	2,235.6 ± 767.7	3,017.8 ± 790.04	< 0.001	< 0.001
Weight	92.71 ± 13.162	92.85 ± 15.648	90.80 ± 14.439	92.11 ± 14.441	0.22	0.48

Table 1. Study characteristics of the adult population.

HBI consists of water, unsweetened coffee and tea, low-fat milk (<1.5% fat, fat free, and/or soy milk), 100% fruit juice, full-fat milk (1.5% fat), and sugar-sweetened beverages (including fruit drinks, sweetened coffee, and tea, soda). Values are mean ± standard deviation or number (percentage). Bold-style p values are considered statistically significant.

HBI, Healthy Beverage Index; BMI, body mass index; WC, waist circumference; WHR, waist hip ratio; FM, fat mass; FFM, fat free mass; BMR, basal metabolic rate. *Crude p value was based on analysis of variance analysis with Tukey's post-hoc comparisons for continuous and χ^2 test when the dependent variable is categorical. [†]The p value derived from one-way analysis of variance with Tukey's post-hoc comparisons after adjustment for confounding factors (age, sex, BMI, physical activity) except energy.

Table 2. Energy-adjusted dietary intakes and tertiles of HBI

Parameters	Tertiles of HBI				p value†
	1st (n = 112)	2nd (n = 113)	3rd (n = 113)		
Vitamin B3 (mg/day)	39 ± 11.7	27.5 ± 6	22.7 ± 8	< 0.001	0.70
Protein (g/day)	132 ± 40	94 ± 18	75.5 ± 25.5	< 0.001	0.78
Fat (g/day)	137 ± 53.5	94 ± 27	73 ± 33	< 0.001	0.22
Carbohydrate (g/day)	615 ± 167	418 ± 66	336 ± 121	< 0.001	0.65
Saturated fatty acid (mg/day)	40 ± 18.5	27.3 ± 8.5	21.4 ± 9.7	< 0.001	0.76
Vitamin A (RAE/day)	$1,142 \pm 694$	854.5 ± 474	728 ± 786	< 0.001	0.39
Vitamin D (µg/day)	2.57 ± 1.85	2.02 ± 1.40	1.54 ± 0.99	< 0.001	0.03
Vitamin E (mg/day)	20.68 ± 7.80	16 ± 8	12 ± 6.1	< 0.001	0.15
Vitamin K (µg/day)	29 ± 48.4	35 ± 22.3	35 ± 51.5	< 0.001	0.15
Vitamin C (mg/day)	323.37 ± 217.50	234.50 ± 131	172 ± 155.5	< 0.001	0.61
Vitamin B12 (µg/day)	6.91 ± 5.60	4.67 ± 4.16	4.53 ± 7.40	< 0.001	0.64
Magnesium (mg/day)	719.3 ± 281.5	513.5 ± 98	411 ± 63	< 0.001	0.03
Iron (mg/day)	32.5 ± 13.5	22 ± 4.5	17.5 ± 6.5	< 0.001	0.98
Zinc (mg/day)	19.8 ± 9	14 ± 3	11 ± 4	< 0.001	0.30
Calcium (mg/day)	$1,766 \pm 0.651$	$1,206 \pm 290$	935 ± 352	< 0.001	0.05
Vitamin B2 (mg/day)	3.5 ± 1	2.5 ± 0.5	2 ± 0.73	< 0.001	0.11

HBI consists of water, unsweetened coffee and tea, low-fat milk (< 1.5% fat, fat free, and/or soy milk), 100% fruit juice, full-fat milk (1.5% fat), and sugar-sweetened beverages (including fruit drinks, sweetened coffee, and tea, soda). Data are presented as mean ± standard deviation. Bold-style p values are considered statistically significant.

HBI. healthy beverage index.

*Crude P values; [†]The p values are from the analysis of covariance with Tukey's post-hoc comparisons (all the variables except energy were adjusted for energy intake).

DISCUSSION

We aimed to describe the progress of a scoring system to assess an individual's beverage consumption in line with current recommendations and assess the relationship between beverage consumption scores and metabolic factors in adults. We showed that HBI can measure a person's overall health concerning the beverages consumed. However, these findings can be



Table 3. Distribution of participants' beverage components

Beverage components	Tertiles of HBI				
	1st (n = 112)	2nd (n = 113)	3rd (n = 113)	Total (n = 338)	
Water	14.64 ± 1.04	15.00 ± 0.00	14.95 ± 0.30	14.88 ± 0.63	0.985
Coffee and tea	4.95 ± 0.48	5.00 ± 0.00	4.82 ± 0.47	4.92 ± 0.39	0.962
Low-fat milk	5.00 ± 0.00	5.00 ± 0.00	5.00 ± 0.00	5.00 ± 0.00	1.00
100% fruit juice	5.00 ± 0.00	5.00 ± 0.00	5.00 ± 0.00	5.00 ± 0.00	1.00
Full-fat milk	5.00 ± 0.00	5.00 ± 0.00	5.00 ± 0.00	5.00 ± 0.00	1.00
Sugar-sweetened beverages	14.09 ± 2.06	14.95 ± 0.46	14.75 ± 1.22	14.61 ± 1.43	0.896
Total beverage energy	0.00 ± 0.00	0.00 ± 0.00	1.36 ± 5.06	0.47 ± 3.06	< 0.001
Met total fluid requirements	6.35 ± 2.56	8.93 ± 1.14	15.77 ± 4.53	10.53 ± 4.99	< 0.001
Total HBI	53.59 ± 3.95	58.89 ± 1.08	66.68 ± 4.81	59.76 ± 6.51	< 0.001

The HBI scores range from 0 to 100, with a higher score indicating a healthier beverage pattern. Data are presented as mean ± standard deviation. Bold-style p values are considered statistically significant.

HBI, Healthy Beverage Index.

*The p value was based on analysis of variance analysis.

Table 4. Biochemical parameters of the study population by tertiles of HBI

Parameters	Tertiles of HBI					p value†
-	1st (n = 112)	2nd (n = 113)	3rd (n = 113)	Total (n = 338)	_	
Participant characteristics						
Serum glucose (mmol/L)	91.74 ± 16.27	93.34 ± 24.68	92.89 ± 15.39	92.667 ± 19.188	0.89	0.81
Insulin (μIU/mL)	15.34 ± 11.42	18.05 ± 17.84	15.22 ± 10.89	16.17 ± 13.66	0.25	0.32
HOMA-IR	3.45 ± 2.48	4.28 ± 4.21	3.58 ± 2.88	3.76 ± 3.26	0.21	0.21
HDL-C (mg/dL)	43.22 ± 9.28	42.44 ± 9.49	44.29 ± 9.75	43.32 ± 9.52	0.13	0.33
LDL-C (mg/dL)	121.89 ± 28.31	127.06 ± 34.31	122.11 ± 32.52	123.68 ± 31.83	0.32	0.37
TC (mg/dL)	189.50 ± 32.32	196.66 ± 39.79	188.23 ± 37.12	191.45 ± 36.64	0.13	0.17
TG (mg/dL)	137.56 ± 57.71	171.74 ± 126.06	139.63 ± 73.08	152.55 ± 94.13	0.01	0.01*
SBP (mmHg)	123.16 ± 19.44	124.01 ± 14.55	121.82 ± 14.89	122.99 ± 18.35	0.59	0.59
DBP (mmHg)	81.10 ± 13.04	82.43 ± 11.53	81.80 ± 10.43	81.78 ± 11.69	0.22	0.69

Data are presented as mean ± standard deviation. Bold-style p values are considered statistically significant.

HBI, Healthy Beverage Index; HOMA-IR, homeostatic model assessment for insulin resistance; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; TC, total cholesterol; TG, triglycerides; SBP, systolic blood pressure; DBP, diastolic blood pressure.

*Crude p values based on analysis of covariance with Tukey's post-hoc comparisons. [†]The p value was based on analysis of covariance with Tukey's post-hoc comparisons was used to compare biochemical variables after adjusting for confounding factors (age; sex; BMI; physical activity).

used as a first step in developing interventions to improve drinking patterns. Few studies have examined the association between HBI and its associated outcomes [35]. In the present study we performed to evaluate the association of HBI with metabolic factors among adults in Tabriz, a positive correlation was seen between higher HBI scores and a more favorable lipid profile and the risk of hypertension [35]. The present study showed a positive association between HBI and weight loss. We also showed that participants in the third tertile of HBI had lower levels of body weight. Reducing macronutrient intake is the highest level of adherence to HBI. A study by Duffey and Davy [35] in the United States on healthy adults aged 18–30 showed that HBI scores were associated with metabolic syndrome. A study of children by Jalilpiran et al. [37] in Tehran showed that HBI scores were associated with weight loss and slimming, indicating consistent results with our study. A single study by Lee and Shin [38] in Korea on adults aged 40–69 showed that receiving healthy drinks led to higher HBI scores and reduced central obesity.

In most cases, the adults in Tabriz consumed the recommended beverages, including coffee, tea, low-fat milk, high-fat milk, 100% natural fruit juice, and all the fluids necessary for the human body. The component that consistently had the highest score for people (i.e., recommended intakes) was low-fat milk. The most distinguished components were the HBI tertiary scores of water (20% to 50% fluid requirements), SSBs (0% to 8% fluid requirements), and total drink energy consumption (10% to 14% of total energy). A range of 10 points in scores to meet water needs indicates that people with the highest HBI scores consume most



of their fluids from water. The higher score range for SSBs and the total energy components of the drink suggest that the recommendations related to these components are the ones that adults in Tabriz are most involved in. Although recent data show that SSB intake has declined, it is estimated that SSBs account for 8% of total daily energy intake [39]. SSBs are a source of minerals the body requires [40], but they have little nutritional value.

Given the public media's emphasis on reducing SSB intake, it is possible that the intake of energy-rich and nutrient-poor beverages has decreased. These changes have not yet helped reduce waist circumference. This result will be unexpected, especially if these changes in beverage consumption are expected recently and/or are not accompanied by other beneficial health behaviors (e.g., decreased total energy expenditure and increased physical activity). Although we control all energy consumption, we did not examine the relationship in more detail using specific macronutrients, as this was beyond the scope of our study. Fluid deficiency is associated with many adverse health outcomes [41,42], and up to a quarter of cardiovascular deaths may be prevented through healthy lifestyle behaviors [43]. HBI provides measurable drinking instructions that improve several important health outcomes. A mechanistic summary of adverse health outcomes of SSB consumption is presented in **Figure 1**.

Although this study indicates a meaningful association between TG levels and HBI, there were no statistically meaningful differences among HBI tertiles in terms of blood pressure,

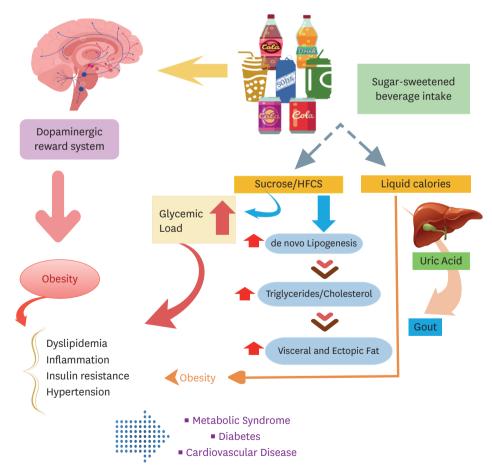


Figure 1. A summary of adverse health effects of sugar-sweetened beverages consumption. HFCS, high-fructose corn syrup.



glucose, insulin-related parameters, HDL-C, and LDL-C, as Rasaei et al. [44] in a crosssectional study on 210 females with obesity observed no significant association between higher HBI scores and the likelihood of abnormal metabolic status.

Our study has limitations, such as selecting components based on evidence-based recommendations [12,35,45]. However, there may have been other important components that we could not consider. Although the scoring system to assign points to individuals is somewhat arbitrary, we tested an alternative scoring system. However, it did not increase our ability to distinguish between components with little variability. As a result, we developed a scoring system that prioritized components that are associated with health outcomes. All cross-sectional studies are susceptible to errors and bias in reporting self-observed and self-reported dietary data. Natural reporting errors that arise when utilizing FFQ, such as improper data classification, is a study limitation that cannot be avoided. Also, the prevalence of SSB consumption in Tabriz and the large volume of study samples were the strengths of the study. Therefore, prospective studies should evaluate these associations over longer periods. The cross-sectional design of this study prevented us from making a definite link between HBI and anthropometric status. According to our information, this is the first study to examine the relationship between HBI and metabolic factors in adults in Tabriz.

CONCLUSION

Our study showed a positive relationship between HBI scores and obesity. Prospective studies are also needed to assess the association between HBI scores and metabolic factors in adults over a long period.

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