The association between dietary total antioxidant capacity and odds and severity of irritable bowel syndrome among Iranian adults: a cross-sectional study

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Abstract

Background: Little evidence is available in terms of the role of dietary antioxidants in the management of irritable bowel syndrome (IBS) disease. This study aimed to examine the association between dietary total antioxidant capacity (dTAC) and odds of IBS and its severity.

Methods: This cross-sectional study was conducted on 3,362 Iranian adults who were referred to health centers of Isfahan province, Iran. Participant's dietary intakes were collected using a semi-quantitative validated food frequency questionnaire (DS-FFQ). dTAC was measured by the ferric-reducing antioxidant power (FRAP) method. Multivariable binary or ordinal logistic regression analyses were performed to estimate any associations between dTAC and odds of IBS and its severity.

Results: The average age and BMI of the participants and dTAC score were 36.3 ± 7.87, 24.9 ± 3.82 and 7.81 ± 3.45, respectively. In crude and adjusted models, the results did not show any significant association between dTAC and odds of IBS among whole and gender-age stratified populations. Being in the third compared with the first category of dTAC was not also significantly associated with odds of IBS severity. Besides, there were no significant associations between dTAC and odds of IBS with constipation, IBS with diarrhea, IBS mixed subtype, and Unsubtyped IBS, respectively.

Conclusion: This study indicates that dTAC may not be associated with odds of IBS and its severity even after stratification for gender and body mass index.

Introduction

Irritable bowel syndrome (IBS) is a highly costed and potentially disabling functional gastrointestinal (GI) disorder that affects 11.2% of populations globally [1]. While there is no documented information about its prevalence in Iran, the results of a cross-sectional study showed that 15% of its population was affected by IBS [2]. Predominant symptoms of this disorder are difficulty in defecation and abdominal pain which may increase with stress [3]. Studies suggest inflammation or injury to tissues as potential causes for the development of symptoms in IBS [4]. In this line, previous research revealed elevated levels of pro-inflammatory cytokines in patients who suffered from this disorder [5, 6]. Evidence suggests that the antioxidants defense system is impaired in IBS which may also play a role in the pathogenesis of the disease [7].

Different pharmacological therapies are used to treat patients with IBS, however, they preferably avoid medications and usually accept other alternative therapies [8]. Previous research has been demonstrated the efficacy of dietary modifications in the management of IBS symptoms. Accordingly, several dietary approaches including diets that remove especial carbohydrates, gluten, substances that might lead to food-related antibodies, and fermentable foods have been suggested to be effective in the treatment of disease [9, 10]. Recent epidemiological studies also assessed the associations of dietary indices, as new tools for the prediction of the associations between dietary habits and disease risk, concerning IBS risk [11–14], however, there is little about the potential role of other components of a diet such as dietary

antioxidants in this context. Because there are interactions among nutrients and synergetic effects of antioxidants in a diet, recent nutritional studies use the dietary total antioxidant capacity (dTAC) index to estimate overall dietary antioxidants in a diet [15]. This index shows the overall capacity of antioxidants in food to protect against free radicals [16]. Also, it can be regarded as an indicator of diet quality [16] as it was positively associated with other dietary quality indices such as Healthy Eating Index, Mediterranean Diet Score, and Diet Quality index [17, 18]. Moreover, studies show that dTAC is a good predictor of plasma antioxidant status [19–21]. Accordingly, several studies have been conducted on the associations between dTAC and chronic disease [22–26]. Also, it has been indicated that dTAC has been inversely associated with plasma levels of high-sensitivity C-reactive protein [27] and plasma malondialdehyde [28], and stress [29] as major risk factors for developing IBS symptoms.

Overall, dietary antioxidants seem to have an inevitable role in the pathogenesis of GI disease, however, only one study has been addressed such an important issue [30]. Also, evidence suggests a nutritional transition from healthy to unhealthy nutritional habits (massive meals, high intake of refined grains, high intake of energy from carbohydrates, and high consumption of hydrogenated oils) among the Iranian population that may relate to such chronic disease [31]. Therefore, we performed this study to evaluate the association between DTAC and odds and severity of IBS symptoms among the Iranian population.

Materials And Methods

Participants

The SEPAHAN project (Epidemiology of Psychological, Alimentary Health and Nutrition) was used as a source of data for this cross-sectional study [32]. The project mainly aimed to find out whether lifestyle and psychological factors have an association with functional GI disorders in adults (18–55 years) in Isfahan province. The SEPAHAN project included non-academic staff, managers and their socio-economic status, and employees who were working in fifty healthcare centers affiliated with Isfahan University of Medical Sciences (IUMS). Isfahan University of Medical Sciences' Bioethics Committee approved the project protocol (Approval No. 189069, 189082, and 189086). All subjects filled out a written informed consent form before participating. A total of 10,087 subjects distributed to complete self-administered questionnaires in phase one of the project, which collected sociodemographic data, anthropometric measurements, medical history, physical activity levels, and dietary intake data. A response rate of 86.16% to the questionnaires was recorded in this phase and 8.691 subjects completed the questionnaires. In the second phase, participants were asked to fill out the questionnaire about gastrointestinal profile. 64.6% of participants provided information about GI health (N = 6239). As a result of combining the data from both phases, we had information on 4,763 subjects' dietary intakes and GI disorders from phase one and tow. Finally, we excluded participants in the final analyses if their daily energy intakes were lower than 800 kcal/d or upper than 4200 kcal/d. After this exclusion 3,362 participants remain for the final analysis.

Dietary Intakes Assessment And Dtac Calculation

We gathered dietary intakes of the study participants using a validated 106-items dish-based semi-quantitative food frequency questionnaire (DS-FFQ) [33]. The DS-FFQ included five categories of food and dishes, including mixed dishes (canned or cooked, 29 items), grains (different kinds of breads, potatoes, cakes, and biscuits, 10 items), fruits and vegetables (22 items), dairy products (dairies, cream, and butter, 9 items), and miscellaneous food items and beverages (including beverages, fast foods, sweets, nuts, and desserts, 36 items). To collect information about these 106 food items, we defined a routine portion size for each and subjects reported their amount of consumption based on nine multiple-choice frequency response categories which were varied from “never or < 1/month” to “≥ 12/day”. Accordingly, 6 to 9 options were available for frequency responses. For foods consumed rarely, we removed the high-frequency category, while we added several multiple-choice categories for foods consumed frequently. According to the frequency of consumption of each food item, grams of each food item were estimated based on household measurements. The ferric-reducing antioxidant power (FRAP) (mmol/100 g) values of each food item in the DS-FFQ were used to calculate DTAC. The FRAP assay is used to measure the ability of total anticipants in a diet that reduces ferric ions to ferrous ones [34]. Accordingly, we calculated the FRAP values for foods based on the previous research [35]. In the case of food items that were similar (e.g., a variety of breads, meats, etc.) or did not have available FRAP values, the values of nearest comparable food were assigned. Then, each frequency consumption for each food item was multiplied by its FRAP value and all summed to obtain dTAC for each person.

Assessment Of Ibs

A version of the Rome III questionnaire, which was developed for the Iranian population, was utilized to measure IBS symptoms. [36]. Because most participants found it difficult to respond to an original questionnaire (never, 1 day per month, 1 day per month, 2–3 days per month, 1 day per week, more than 1 day per week, and every day), we used a questionnaire with a 4-item rating scale (never/rarely, sometimes, often, and always). Each symptom's long-term experience (six months or more) was replaced with a shorter-term experience (less than three months) [37]. Subjects has IBS if they experienced abdominal discomfort or pain before the initiation of study sometimes (in the last three months) along with at least two or more of the following criteria; improvement in abdominal discomfort or pain with defecation sometimes and the onset of such condition related to changes in stool frequency or form [38]. Constipation-predominant IBS was identified if they had hard or lumpy stools, as well as a lack of loose, mushy, or watery stools. [39]. If they had watery stools and no firm stools on a regular basis, they had diarrhea-predominant IBS [40]. The subjects were considered to have mixed IBS if they had IBS, hard or lumpy stools at least sometimes, and loose, mushy, or watery stools at least sometimes [41]. Other participants were considered as unshaped kind of IBS. The severity of abdominal pain in the last three months was also reported by the subjects and classified as mild, moderate, severe, and very severe.

Assessment Of Other Lifestyle Factors

We collected information on other lifestyle factors such as age, sex, smoking history, marital status, medication use, and disease history through a self-reported questionnaire. A number of anthropometric measurements were taken, including weight, height, and waist circumference and Body mass index (BMI) was estimated by dividing of weight in kg by height in square of meter (kg/m^2). A pilot study on a sample of 200 participants found reasonable results for the usefulness of these self-reported anthropometric measures. The results showed statistically significant correlation coefficient for weight 0.95 ($P < 0.001$), height 0.83 ($P < 0.001$), WC 0.60 ($P < 0.001$), and BMI 0.70 ($P < 0.001$) from these self-reported values compared to the measured values [42]. The General Practice Physical Activity Questionnaire (GPPAQ) was also completed by the subjects to assess physical activity levels. Accordingly, subjects were classified as physically inactive (< 1 h/week) and physically active (≥ 1 h/week). Also, intra-meal fluid intake (< 3 glasses/≥3 glasses), meal regularity (often or frequently or always and never or rarely), and chewing efficiency (a lot/not a lot) were evaluated through a pretested questionnaire. The subject's dental status was assessed based on four different categories ("fully dentate", "lost 1–5 teeth", and "lost > 5 teeth"). Finally, we gathered information on dietary supplement usage (yes/no), oral contraceptives drugs usage (yes/no), and the presence of colitis (yes/no).

Statistical analysis

In this study, we classified participants according to tertile cut-off points of dTAC score. One way ANOVA and chi-square tests were used to compare the differences of general characteristics of participants across tertiles of dTAC. We used the analysis of covariance (ANCOVA) test for comparison of energy-adjusted dietary intakes of participants across tertiles of dTAC. A binary logistic regression test was used to estimate odd ratios and 95% CIs of IBS and its subtypes across tertiles of dTAC in crude and multivariable-adjusted models. In the analyses, models were adjusted for age, sex, energy intake, marital status, education, BMI, physical activity, diabetes history, medication use, smoking, meal regularity, dietary supplements use, chewing sufficiency, frequency of fried food consumption, speed of eating, dental status, intra-meal fluid consumption, and breakfast skipping). We also estimated ORs and 95% CIs for IBS severity (mild, moderate, severe, and very severe) across tertiles of dTAC multivariable ordinal logistic regression. SPSS software (version 24; SPSS Inc.) was used for data analysis and $P < 0.05$ was considered as statistically significant.

Results

In this cross-sectional study, the average age and BMI of the participants were 36.3 ± 7.87 and 24.9 ± 3.82. The dTAC mean was 7.81 ± 3.45 and ranged from 0.57 to 23.72. General features of the study participants as well as the rate of the prevalence of IBS and its subtypes across tertiles of dTAC are presented in Table 1. Accordingly, participants in the highest tertile of dTAC score were older ($p < 0.001$) and had higher education levels ($p < 0.001$) and had greater adherence to a regular meal pattern ($p <$

0.001) than those in the lowest tertile. We did not find any significant findings in terms of other characteristics across tertiles of dTAC score.

Table 1
Baseline Characteristics of study participants as well as the prevalence of IBS and its subtypes across tertiles of dTAC [a].

Variables	Tertiles of dTAC			P-value [b]
	T1 (< 6.06)	T2 (6.06–8.96)	T3 (≥ 8.96)	
dTAC	4.30 ± 1.32	7.48 ± 0.83	11.65 ± 2.46	< 0.001
Age (y)	35.6 ± 7.79	36.1 ± 7.92	37.2 ± 7.82	< 0.001
BMI (kg/m2)	24.8 ± 3.92	24.9 ± 3.72	25.0 ± 3.82	0.44
Female (%)	648 (57.9)	641 (57.2)	670 (59.8)	0.44
Married (%)	900 (82.5)	901 (82.0)	889 (80.6)	0.80
Education (university graduated) (%)	637 (56.9)	707 (63.1)	737 (65.7)	< 0.001
Physically active c (%)	136 (12.1)	147 (13.1)	160 (14.3)	0.33
Current smoker (%)	150 (13.4)	150 (13.4)	164 (14.6)	0.62
Regular meal pattern				< 0.001
Never/sometimes	501 (45.7)	419 (37.8)	395 (35.7)	
Often/always	596 (54.3)	689 (62.2)	712 (64.3)	
Chewing sufficiently (a lot)	128 (11.6)	145 (13.1)	158 (14.2)	0.19
Fluid Consumption				0.29
< 3 glasses/day	1054 (96.2)	1059 (96.8)	1064 (97.3)	
≥ 3 glasses/day	42 (3.8)	35 (3.2)	29 (2.7)	

IBS-C: IBS with constipation; IBS-D: IBS with diarrhea; IBS-M: mixed IBS; IBS-U: unsubtyped IBS.

[a] Data are mean ± SD, unless indicated otherwise.

[b] Obtained from ANOVA or chi-square test, where appropriate.

[c] ≥ 1 hour/week physical activity.

[d] Chronic disease included: diabetes and colitis.

[e] Medications included omeprazole, pantoprazole, ranitidine, cimetidine, famotidine, clidinium, hyoscine, blandola, dimethicone, digestive, pancreatin, antiacid, diphenoxylate, loperamide, nortriptyline, amitriptyline or imipramine, fluoxetine, citalopram, fluvoxamine, and sertraline.

[f] Dental status > 5 teeth lost.

Variables	Tertiles of dTAC			P-value [b]
	T1 (< 6.06)	T2 (6.06–8.96)	T3 (≥ 8.96)	
Breakfast skipping	89 (8.3)	73 (6.7)	76 (7.0)	0.29
Frequent fried food intake				0.56
≤ 3 times/wk	917 (85.4)	920 (84.6)	909 (83.7)	
>3 times/wk	157 (14.6)	168 (15.4)	177 (16.3)	
Speed of eating				0.29
< 10 minutes	109 (9.7)	92 (8.2)	112 (10.0)	
≥ 10 minutes	1011 (90.3)	1029 (91.8)	1009 (90.0)	
Disease history [d] (%)	35 (3.1)	34 (3.0)	31 (2.8)	0.87
Medication use [e] (%)	70 (6.3)	59 (5.3)	75 (6.7)	0.35
Dietary supplement use (%)	339 (30.3)	320 (28.5)	350 (31.2)	0.37
Dental status [f] (%)	81 (7.4)	77 (7.1)	96 (8.9)	0.57
IBS (%)	256 (22.9)	252 (22.5)	240 (21.4)	0.69
IBS-C (%)	93 (8.3)	73 (6.5)	87 (7.8)	0.26
IBS-D (%)	51 (4.6)	52 (4.6)	53 (4.7)	0.98
IBS-M (%)	46 (4.1)	45 (4.0)	38 (3.4)	0.63
IBS-U (%)	66 (5.9)	82 (7.3)	62 (5.5)	0.18

IBS-C: IBS with constipation; IBS-D: IBS with diarrhea; IBS-M: mixed IBS; IBS-U: unsubtyped IBS.

[a] Data are mean ± SD, unless indicated otherwise.

[b] Obtained from ANOVA or chi-square test, where appropriate.

[c] ≥ 1 hour/week physical activity.

[d] Chronic disease included: diabetes and colitis.

[e] Medications included omeprazole, pantoprazole, ranitidine, cimetidine, famotidine, clidinium, hyoscine, blandola, dimethicone, digestive, pancreatin, antiacid, diphenoxylate, loperamide, nortriptyline, amitriptyline or imipramine, fluoxetine, citalopram, fluvoxamine, and sertraline.

[f] Dental status > 5 teeth lost.

Table 2 shows dietary intakes of participants across tertiles of dTAC. A greater dTAC score was significantly associated with higher energy intake, carbohydrates, dietary fibers, saturated fatty acids, some vitamin A, vitamin C, vitamin B6, vitamin B9, calcium, fruits, vegetables, whole grains, tea and coffee, and pickles. It was also significantly associated with lower intakes of protein, fats, vitamin E, vitamin B1, vitamin B12, Fe, zinc, white meat, red and processed meat, and refined grains.

Table 2

Dietary intakes of study participants across tertiles of dTAC [a].

	Tertiles of dTAC			P-value [b]
	T1 (N = 971)	T2 (N = 1008)	T3 (N = 1008)	
Nutrients				
Energy intake (kcal/d)	1842.0 ± 22.6	2426.0 ± 22.1	2859.9 ± 22.2	< 0.001
Carbohydrate (g/d)	280.4 ± 1.64	294.4 ± 1.48	306.8 ± 1.59	< 0.001
Protein g/d)	91.2 ± 0.47	88.3 ± 0.42	85.4 ± 0.46	< 0.001
Fat (g/d)	102.0 ± 0.64	98.2 ± 0.57	95.7 ± 0.62	< 0.001
Fiber (g/d)	20.1 ± 0.19	22.3 ± 0.17	25.3 ± 0.18	< 0.001
SFA (g/d)	18.8 ± 7.61	23.8 ± 9.00	26.9 ± 8.92	0.01
Vitamin A (RAE/d)	480.3 ± 7.00	517.3 ± 6.29	559.6 ± 6.77	< 0.001
Vitamin C (mg/day)	74.5 ± 1.66	99.3 ± 1.50	130.3 ± 1.61	< 0.001
Vitamin D (µg/d)	0.97 ± 0.01	0.96 ± 0.02	0.97 ± 0.02	0.70
Vitamin E (mg/d)	22.7 ± 0.20	21.1 ± 0.18	20.6 ± 0.20	< 0.001
Vitamin B1 (mg/d)	1.86 ± 0.02	1.89 ± 0.02	1.79 ± 0.02	< 0.001
Vitamin B6 (mg/d)	1.94 ± 0.01	1.97 ± 0.01	2.03 ± 0.01	< 0.001
Folate (µg/day)	286.0 ± 2.50	317.1 ± 2.25	358.1 ± 2.42	< 0.001
Vitamin B12 (µg/day)	3.04 ± 0.04	2.97 ± 0.03	2.87 ± 0.03	0.01
Calcium (mg/day)	965.7 ± 14.7	1012.2 ± 13.2	962.5 ± 14.2	0.01
Fe (mg/day)	18.0 ± 0.11	17.8 ± 0.10	17.1 ± 0.11	< 0.001
Zinc (mg/day)	11.3 ± 0.06	11.1 ± 0.05	10.9 ± 0.06	< 0.001
Food groups				
Fruits (g/d)	177.3 ± 7.07	301.9 ± 6.35	469.0 ± 6.84	< 0.001
Vegetables (g/d)	219.7 ± 4.07	237.5 ± 3.65	259.9 ± 3.93	< 0.001
White meat (g/d)	69.4 ± 1.51	62.6 ± 1.36	58.9 ± 1.46	< 0.001

a Data are means ± standard error (SE), unless indicated.

b * All values were adjusted for age, sex and energy, except for dietary energy intake, which was only adjusted for age and sex using ANCOVA.

	Tertiles of dTAC			P-value [b]
	T1 (N = 971)	T2 (N = 1008)	T3 (N = 1008)	
Red and processed meat (g/d)	92.6 ± 1.55	82.7 ± 1.39	78.08 ± 1.49	< 0.001
Nuts, legumes and soy (g/d)	59.1 ± 1.26	56.0 ± 1.13	56.6 ± 1.22	0.18
Refined grains (g/d)	438.9 ± 5.60	403.2 ± 5.03	338.2 ± 5.41	< 0.001
Whole grains (g/d)	34.1 ± 2.62	42.2 ± 2.36	51.1 ± 2.54	< 0.001
Dairy intake (g/d)	331.6 ± 9.10	356.6 ± 8.20	357.5 ± 8.80	0.09
Tea and coffee (g/d)	158.0 ± 8.08	355.7 ± 7.26	625.3 ± 7.82	< 0.001
Pickles (g/d)	7.10 ± 0.61	8.90 ± 0.55	10.84 ± 0.59	< 0.001
a Data are means ± standard error (SE), unless indicated.				
[b] * All values were adjusted for age, sex and energy, except for dietary energy intake, which was only adjusted for age and sex using ANCOVA.				

Multivariable-adjusted ORs and 95% CIs for IBS across tertile categories of dTAC were shown in Table 3. In crude model, the results did not show any significant association between dTAC and odds of IBS among whole population (OR = 0.92; 95% CI= (0.75–1.12); P_{trend} = 0.41). After adjustment for confounders in different models the results remained non-significant. Stratified analyses based on the gender ((male: OR = 0.94; 95% CI= (0.67–1.31); P trend = 0.73), female: (OR = 0.90; 95% CI= (0.75–1.24); P_{trend} = 0.39)) and BMI ((BMI < 25 (kg/m^2): OR = 0.80; 95% CI= (0.60–1.42); P trend = 0.13), BMI≥25 (kg/m^2): (OR = 1.05; 95% CI= (0.77–1.42); P trend = 0.75)) also did not reveal any significant associations in crude model. These findings were also remained non-significant even after adjustment for potential confounders.

Table 3
Gender- and BMI-stratified ORs and 95% CIs for IBS across tertiles of dTAC.

	Tertiles of dTAC			P-trend
	T1 (< 6.06)	T2 (6.06–8.96)	T3 (≥ 8.96)	
	OR	OR (95% CI)	OR (95% CI)	
Whole population				
Crude	1.00	0.98 (0.80–1.19)	0.92 (0.75–1.12)	0.41
Model 1 [a]	1.00	1.08 (0.87–1.36)	1.12 (0.88–1.44)	0.35
Model 2	1.00	1.11 (0.88–1.39)	1.11 (0.86–1.43)	0.43
Model 3	1.00	1.15 (0.90–1.46)	1.12 (0.86–1.46)	0.42
Model 4	1.00	1.09 (0.85–1.39)	1.07 (0.81–1.40)	0.64
Male				
Crude	1.00	1.01 (0.73–1.39)	0.94 (0.67–1.31)	0.73
Model 1 [b]	1.00	1.33 (0.90–1.97)	1.40 (0.91–2.15)	0.13
Model 2	1.00	1.28 (0.86–1.91)	1.31 (0.85–2.03)	0.23
Model 3	1.00	1.56 (1.02–2.39)	1.52 (0.95–2.43)	0.09
Model 4	1.00	1.47 (0.95–2.27)	1.39 (0.86–2.24)	0.21
Female				
Crude	1.00	0.97 (0.75–1.24)	0.90 (0.75–1.24)	0.39
Model 1 [b]	1.00	0.99 (0.75–1.30)	1.01 (0.75–1.37)	0.94
Model 2	1.00	1.03 (0.78–1.36)	1.01 (0.74–1.38)	0.95
Model 3	1.00	1.01 (0.75–1.35)	0.96 (0.69–1.34)	0.83

Model 1 [a]: adjusted for age, gender, and energy intake.

Model 1 [b]: adjusted for age

Model 2: further adjusted for physical activity, marital status, education level, smoking, chronic disease, medication use and dietary supplement intake.

Model 3: further adjusted for regular meal pattern, eating rate, chewing sufficiency, breakfast skipping, fluid consumption, fried food intake, and dental status.

Model 4: additionally, adjusted for BMI

	Tertiles of dTAC			P-trend
	T1 (< 6.06)	T2 (6.06–8.96)	T3 (⩾ 8.96)	
	OR	OR (95% CI)	OR (95% CI)	
Model 4	1.00	0.96 (0.71–1.29)	0.95 (0.68–1.32)	0.77
BMI < 25 (kg/m2)				
Crude	1.00	1.09 (0.83–1.42)	0.80 (0.60–1.42)	0.13
Model 1 [a]	1.00	1.19 (0.87–1.62)	1.02 (0.72–1.44)	0.91
Model 2	1.00	1.21 (0.88–1.66)	1.01 (0.71–1.43)	1.00
Model 3	1.00	1.19 (0.85–1.66)	1.00 (0.69–1.45)	0.97
BMI ≥ 25 (kg/m2)				
Crude	1.00	0.90 (0.66–1.23)	1.05(0.77–1.42)	0.75
Model 1 [a]	1.00	1.04 (0.73–1.47)	1.25 (0.85–1.83)	0.25
Model 2	1.00	1.03 (0.72–1.47)	1.21 (0.82–1.79)	0.33
Model 3	1.00	1.13 (0.78–1.63)	1.25 (0.82–1.88)	0.30
Model 1 [a]: adjusted for age, gender, and energy intake.				
Model 1 [b]: adjusted for age				
Model 2: further adjusted for physical activity, marital status, education level, smoking, chronic disease, medication use and dietary supplement intake.				
Model 3: further adjusted for regular meal pattern, eating rate, chewing sufficiency, breakfast skipping, fluid consumption, fried food intake, and dental status.				
Model 4: additionally, adjusted for BMI				

The results of the analyses on the association between dTAC and odds of IBS severity are provided in Table 4. Accordingly, being in the third compared with the first category of dTAC was not significantly associated with odds of IBS severity in crude model among the whole population (OR = 0.88; 95% CI= (0.67–1.15). When the analyses controlled for several potential confounders, we failed to find any significant association, too. No significant associations were found when the analyses stratified by gender ((male: OR = 0.90; 95% CI= (0.56–1.45), female: (OR = 0.87; 95% CI= (0.63–1.20)) and BMI ((BMI < 25 (kg/m2): (OR = 0.91; 95% CI= (0.63–1.33), BMI ≥ 25 (kg/m2): (OR = 0.77; 95% CI= (0.51–1.17)) in crude model. These results were also found when the analyses controlled for potential confounders.

Table 4
Gender- and BMI-stratified ORs and 95% CIs for IBS severity across tertiles of dTAC.

	Tertiles of dTAC		
	T1 (< 6.06)	T2 (6.06–8.96)	T3 (≥ 8.96)
	OR	OR (95% CI)	OR (95% CI)
Whole population			
Crude	1.00	0.90 (0.69–1.17)	0.88 (0.67–1.15)
Model 1 [a]	1.00	0.86 (0.64–1.16)	0.86 (0.62–1.19)
Model 2	1.00	0.90 (0.66–1.21)	0.83 (0.60–1.16)
Model 3	1.00	0.93 (0.67–1.28)	0.87 (0.61–1.25)
Model 4	1.00	0.93 (0.67–1.27)	0.82 (0.57–1.18)
Male			
Crude	1.00	1.10 (0.70–1.74)	0.90 (0.56–1.45)
Model 1 [b]	1.00	0.98 (0.58–1.68)	0.85 (0.47–1.53)
Model 2	1.00	0.90 (0.52–1.56)	0.74 (0.40–1.36)
Model 3	1.00	0.94 (0.51–1.74)	0.74 (0.38–1.46)
Model 4	1.00	0.88 (0.47–1.65)	0.73 (0.90–1.47)
Female			
Crude	1.00	0.81 (0.58–1.22)	0.87 (0.63–1.20)
Model 1 [b]	1.00	0.80 (0.56–1.14)	0.85 (0.57–1.26)
Model 2	1.00	0.88 (0.61–1.26)	0.84 (0.56–1.25)
Model 3	1.00	0.89 (0.61–1.31)	0.92 (0.60–1.41)

Model 1 [a]: adjusted for age, gender, and energy intake.

Model 1 [b]: adjusted for age

Model 2: further adjusted for physical activity, marital status, education level, smoking, chronic disease, medication use and dietary supplement intake.

Model 3: further adjusted for regular meal pattern, eating rate, chewing sufficiency, breakfast skipping, fluid consumption, fried food intake, and dental status.

Model 4: additionally, adjusted for BMI

	Tertiles of dTAC		
	T1 (< 6.06)	T2 (6.06–8.96)	T3 (≥ 8.96)
	OR	OR (95% CI)	OR (95% CI)
Model 4	1.00	0.91 (0.62–1.34)	0.85 (0.55–1.32)
BMI < 25 (kg/m2)			
Crude	1.00	0.96 (0.67–1.39)	0.91 (0.63–1.33)
Model 1 [a]	1.00	0.85 (0.56–1.29)	0.85 (0.54–1.33)
Model 2	1.00	0.94 (0.61–1.43)	0.82 (0.52–1.30)
Model 3	1.00	1.14 (0.72–1.79)	0.96 (0.59–1.58)
BMI ≥ 25 (kg/m2)			
Crude	1.00	0.81 (0.54–1.21)	0.77 (0.51– 1.17)
Model 1 [a]	1.00	0.80 (0.51–1.25)	0.81 (0.49–1.35)
Model 2	1.00	0.76 (0.48–1.22)	0.83 (0.49–1.39)
Model 3	1.00	0.69 (0.42–1.14)	0.73 (0.42–1.30)
Model 1 [a]: adjusted for age, gender, and energy intake.			
Model 1 [b]: adjusted for age			
Model 2: further adjusted for physical activity, marital status, education level, smoking, chronic disease, medication use and dietary supplement intake.			
Model 3: further adjusted for regular meal pattern, eating rate, chewing sufficiency, breakfast skipping, fluid consumption, fried food intake, and dental status.			
Model 4: additionally, adjusted for BMI			

In Table 5 ORs and 95% CIs for IBS subtypes across tertiles of dTAC were presented. In crude model, there was no significant associations between dTAC and odds of IBS-C (OR = 0.93; 95% CI= (0.68–1.26); P trend = 0.63), IBS-D (OR = 1.04; 95% CI= (0.70–1.54); P trend = 0.84), IBS-M (OR = 0.82; 95% CI= (0.53–1.27); P trend = 0.38), and IBS-U (OR = 0.93; 95% CI= (0.65–1.34); P trend = 0.72), respectively. We could not see any significant association even after adjustment for potential confounders.

Table 5
Crude and multivariable-adjusted ORs and 95% CIs for IBS subtypes across tertiles of dTAC.

	Tertiles of dTAC			P-trend
	T1 (< 6.06)	T2 (6.06–8.96)	T3 (≥ 8.96)	
	OR	OR (95% CI)	OR (95% CI)	
IBS-C				
Crude	1.00	0.77 (0.56–1.06)	0.93 (0.68–1.26)	0.63
Model 1	1.00	0.75 (0.52–1.08)	0.99 (0.68–1.45)	0.99
Model 2	1.00	0.76 (0.52–1.09)	0.95 (0.64–1.40)	0.82
Model 3	1.00	0.73 (0.50–1.07)	0.92 (0.62–1.39)	0.71
Model 4	1.00	0.69 (0.46–1.01)	0.90 (0.60–1.37)	0.64
IBS-D				
Crude	1.00	1.02 (0.69–1.51)	1.04 (0.70– 1.54)	0.84
Model 1	1.00	1.24 (0.79–1.96)	1.39 (0.85–2.28)	0.19
Model 2	1.00	1.23 (0.78–1.96)	1.42 (0.86–2.33)	0.17
Model 3	1.00	1.35 (0.84–2.19)	1.52 (0.90–2.56)	0.12
Model 4	1.00	1.39 (0.86–2.25)	1.43 (0.84–2.43)	0.20
IBS-M				
Crude	1.00	0.98 (0.64–1.48)	0.82 (0.53–1.27)	0.38
Model 1	1.00	0.95 (0.59–1.51)	0.89 (0.53–1.50)	0.66
Model 2	1.00	0.95 (0.59–1.52)	0.89 (0.52–1.51)	0.66
Model 3	1.00	1.16 (0.70–1.92)	1.08 (0.61–1.90)	0.80
Model 4	1.00	1.11 (0.67–1.85)	1.01 (0.57–1.79)	0.98

IBS-C: IBS with constipation; IBS-D: IBS with diarrhea; IBS-M: mixed IBS; IBS-U: unsubtyped IBS.

Model 1: adjusted for age, gender, and energy intake.

Model 2: further adjusted for physical activity, marital status, education level, smoking, chronic disease, medication use and dietary supplement intake.

Model 3: further adjusted for regular meal pattern, eating rate, chewing sufficiency, breakfast skipping, fluid consumption, fried food intake, and dental status.

Model 4: additionally, adjusted for BMI

	Tertiles of dTAC			P-trend
	T1 (< 6.06)	T2 (6.06–8.96)	T3 (⩾ 8.96)	
	OR	OR (95% CI)	OR (95% CI)	
IBS-U				
Crude	1.00	1.26 (0.90–1.76)	0.93 (0.65–1.34)	0.72
Model 1	1.00	1.56 (1.06–2.27)	1.21 (0.78–1.87)	0.42
Model 2	1.00	1.60 (1.09–2.34)	1.19 (0.76–1.85)	0.46
Model 3	1.00	1.53 (1.03–2.29)	1.07 (0.67–1.72)	0.78
Model 4	1.00	1.43 (0.95–2.15)	1.05 (0.65–1.70)	0.72
IBS-C: IBS with constipation; IBS-D: IBS with diarrhea; IBS-M: mixed IBS; IBS-U: unsubtyped IBS.				
Model 1: adjusted for age, gender, and energy intake.				
Model 2: further adjusted for physical activity, marital status, education level, smoking, chronic disease, medication use and dietary supplement intake.				
Model 3: further adjusted for regular meal pattern, eating rate, chewing sufficiency, breakfast skipping, fluid consumption, fried food intake, and dental status.				
Model 4: additionally, adjusted for BMI				

Discussion

In the current study, we failed to find significant association between dTAC and odds of IBS in both crude and adjusted models. The results also did not show any associations between dTAC and odds of the severity of the disease and its subtypes. Moreover, no significant associations were found even after stratification by gender and BMI which altogether point out the fact that there may be no associations between the overall antioxidant capacity of the diet and odds of IBS and IBS severity.

The IBS as a multifactorial painful chronic GI disorder is identified by alterations in bowel habits [43]. Evidence showed potential role for inflammation in the occurrence of visceral hypersensitivity which is an important cause for pain and GI discomforts in patients with IBS [4]. In this line, the studies indicated the elevated amounts of pro-inflammatory cytokines in IBS patients compared to the healthy control groups [44, 45]. On the other side, there is a proposed linkage between inflammation and oxidative stress as reactive oxygen species (ROS) is produced by resident cells (endothelial and vascular smooth muscle cell) through leukocytes activation [46]. The results of previous research also demonstrated altered oxidant-antioxidant balance in patients with IBS compared to the healthy controls; so that in those studies the serum levels of prooxidant compounds increased and the serum levels of antioxidant

compounds decreased [7, 45]. Nevertheless, our study for the first time showed that overall dietary antioxidants, estimating using dTAC score, was not significantly associated with odds of IBS and its severity in a large sample size study among the Iranian population. Although there is no similar study that directly addressed such association, however, other studies have been investigated the associations between dTAC and other GI disorders and showed inconsistent results [30, 47–49]. Accordingly, in a case-control study including 62 IBD patients and 124 healthy controls of the Iranian population highest versus lowest quartile of dTAC was significantly associated with a reduced risk of ulcerative colitis [30]. Of course, that study had a different design, and its analyses were not controlled for dietary antioxidant supplements used as an important source of antioxidants in a diet. The Evidence of European Prospective Investigation into Cancer (EPIC) study on 521,457 subjects from 10 European countries showed that highest versus lowest quintile of both FRAP and TRAP, as indicators of dietary antioxidant capacity, was significantly associated with a reduction in the risk of gastric cancer [49]. A case-control study including 1,953 patients with colorectal cancer and 4,154 controls demonstrated an inverse association between FRAP, TEAP, and TRAP with the risk of colorectal cancer in Italian populations [48]. Nevertheless, the results of the Health Professionals Follow-up Study showed that dTAC was not significantly associated with colorectal or colon cancer but was inversely associated with risk incidence of rectal cancer. Interestingly, total antioxidant capacity (from both foods and supplements) was not associated with colorectal, colon, and rectal cancer [47]. Taken tighter, it seems there are limited data to decide about the possible roles of dTAC with the odds and severity of IBS because there is no similar study among other populations and the process of the IBS disease is not fully comparable to other GI disorders. In addition, the results of previous research pointed out the fact that there is little evidence about the inadequacy of single antioxidant-rich food or nutrient in patients with IBS. For example, the results of a case-control study (187 IBS patients and 374 age and gender-matched controls) among the Sweden population showed that IBS patients had a significantly higher intake of vitamin C, B9, Iron, vitamin E, and dietary fiber as well as lower intake of B2, vitamin A, potassium, and calcium compared to the control group. This study also demonstrated that daily nutrient intake in IBS patients met national nutrients recommendations and no association was found between the nutrient intake and IBS subtypes or IBS symptom severity [50]. This finding also has been proven in the previous researches [51–54] and is against the results of the researches that believed dietary restrictions among IBS patients could lead to the lower intake of essential nutrients [55–57]. Our results about the non-significant association between dTAC and odds of IBS may also confirm by studies that evaluated serum oxidative stress markers [45, 58]. Interestingly, in a study on 90 IBS patients and 90 genders and age-matched healthy controls, the researchers found significant and non-significant associations between inflammatory cytokines and oxidative stress biomarkers with digestive symptoms and quality of life in IBS patients, respectively [45]. A review was also conducted on the available data to explore the possible relevance of oxidative stress status in the pathogens of IBS. The authors concluded that there is a possible correlation between some complications such as mild inflammatory patterns, neurological impairment, and emotional over-responsiveness and oxidative stress in IBS patients while are not followed by tissue destruction. Moreover, they suggested that it is not yet clear whether neurological inflammation, impairments, or oxidative stress are key determinants or in which way these three interact in IBS pathology; as well as

there is a need to find possible explanations for the occurrence of oxidative imbalances and its role in the pathogenesis of IBS [58]. So, our results along with reviewing the available data indicate that there is still a need for more comprehensive prospective or clinical trial studies to elucidate the potential role of antioxidants especially dietary ones in the management of IBS.

This cross-sectional study has several strengths. This was the first study investigating the association between dTAC and odds of IBS and its severity. The study design was based on the general population and its sample size was high that reduces the risk of selection bias and the risk of type II error and increases internal validity, respectively. Because the study was conducted on a general population, it included subjects of all grades of IBS and who visited or did not visit a doctor. Since there were heterogeneous characteristics within the IBS population in this study, the results cannot be compared with those of studies involving the merely referred participants. We also controlled the analyses for several confounders. Another advantage of the study is the use of the FRAP index to estimate dTAC as the FRAP test is the only one that directly measures antioxidants in food samples. In some assays, measurement of inhibition depends on the kind of reactive species used in the reaction mixture, while in other assays, the inhibition is dependent on free radicals generated in the reaction mixture. So, they indirectly estimate dTAC [59].

Our study similar to any other study has also had some limitations that should be taken into account. This had a cross-sectional design thus we can't infer the causality of possible relationships between dTAC and IBS. Information about the IBS and its severity was obtained through Rome III questionnaire. Although the questionnaire was validated in Iranian adults, however, it's possible that misclassification did not eliminate. The participants were from Isfahan province; thus, the results should be cautiously generalized to other populations in Iran. Although the analyses were controlled for several confounders, likely residual confounding is inevitable. We had no information about FRAP values of local foods in Iran. Accordingly, this information was derived from international databases which were different from Iranian foods. Finally, although dietary FRAP scores have an advantage compared with other indexes, however, previous evidence did not confirm their relationships with plasma FRAP measurements [20, 21]. These findings may be justified by differences in endogenous antioxidants homeostasis and factors that affect dietary antioxidants absorption or metabolism [60].

Conclusion

The present study indicates that dTAC may not be associated with the odds of occurrence of IBS and its severity. In addition, by reviewing previous research we could not infer about the possible roles of dietary or plasma antioxidants in the pathogenesis of IBS. So, further prospective studies or clinical trials can help to elucidate the existence of any possible associations.

Abbreviations

Analysis of covariance (ANCOVA)

Body mass index (BMI)

Dietary total antioxidant capacity (dTAC)

Evidence of European Prospective Investigation into Cancer (EPIC)

Epidemiology of Psychological, Alimentary Health and Nutrition (SEPAHAN)

Ferric-reducing antioxidant power (FRAP)

General Practice Physical Activity Questionnaire (GPPAQ)

Gastrointestinal (GI)

Irritable bowel syndrome (IBS)

Isfahan University of Medical Sciences (IUMS)

Semi-quantitative validated food frequency questionnaire (DS-FFQ)

Declarations

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Authors' contributions

SS, FS, AA, AHK, AE, and PA contributed to the conception, design, data collection, statistical analyses, data interpretation, manuscript drafting, approval of the final version of the manuscript and agreed for all aspects of the work.

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Availability of data and materials

The data are not publicly available.

Ethics approval and consent to participate

This study was ethically approved by Isfahan University of Medical Sciences' Bioethics Committee (Approval No. 189069, 189082, and 189086)

Consent for publication

Not applicable.

Competing interests

The authors have no competing interests.

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