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Empirically derived food-based inflammatory potential of the diet, irritable bowel syndrome, and its severity

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ABSTRACT

Objective: To our knowledge, no studies have examined the association between the empirically derived food-based dietary inflammatory index (FDII) and irritable bowel syndrome (IBS). The aim of this study was to examine the relationship between the FDII score and IBS in a large sample of Iranian adults.
Methods: In this cross-sectional study, the dietary intakes of 3363 adults were assessed using a validated dish-based 106-item semi-quantitative food frequency questionnaire (DS-FFQ). The FDII was calculated based on the dietary intakes of food groups derived from DS-FFQ. IBS was assessed using a modified Persian version of the Rome III questionnaire.
Results: Participants in the top quintile of the FDII score had a 42% greater risk for IBS than those in the bottom quintile (odds ratio [OR], 1.42; 95% confidence interval [CI], 1.08–1.88). Among women, we observed a significant direct association between the FDII score and IBS after adjustment for potential confounders (OR, 1.44; 95% CI, 1.01–2.04). By body mass index (BMI) status, normal weight subjects (BMI <25 kg/m^2) in the top quintile of the FDII score had higher risk for IBS (OR, 1.60; 95% CI, 1.07–2.35) than those in the bottom quintile. These associations were not observed in men or in participants with a BMI ≥25 kg/m^2. There was no significant association between the FDII score and IBS subtypes. No significant association between the FDII score and IBS severity was observed.
Conclusions: Consumption of a pro-inflammatory diet was associated with increased risk for IBS, especially in women and in individuals with a BMI <25 kg/m^2.

Introduction

Irritable bowel syndrome (IBS) is a gastrointestinal (GI) chronic functional disorder [1] that results in substantial costs to patients, the health care system, and society [2,3]. More than 10% to 15% of the US population and 10.9% of Iranian adults are affected by this syndrome [4,5]. According to previous studies, IBS is more prevalent in women than men [1].

Given the role of diet in the management of IBS as a pro-inflammatory state [6,7], examining the contribution of inflammatory potential of the diet in this condition is priority. The dietary inflammatory index (DII) has been developed to assess the inflammatory potential of the diet [8]. An earlier version of this index was developed mainly based on nutrients. Recently, Tabung et al. developed an empirically derived dietary inflammatory index (FDII) based on food groups [9]. Although the nutrient-based DII can provide valuable information about the inflammatory potential of the diet, nutrients are consumed in combination, not separately. Therefore,

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they might have interaction or synergistic effects on each other in the lumen. In addition, to increase the adherence to dietary recommendations, they should be based on foods or food groups rather than on nutrients. Some previous investigations have examined the association between the FDII and risk for chronic conditions including ovarian and colorectal cancers [10,11]. However, little attention has been given to IBS. The present study aimed to investigate the association between FDII and prevalence of IBS and its severity in a large population of Iranian adults.

Materials and methods

Participants

This cross-sectional study was conducted within the framework of the SEPAHAN (Study on the Epidemiology of Psychological, Alimentary Health and Nutrition) project, a cross-sectional study that investigated the prevalence of functional GI disorders (FGIDs) and their relationship to lifestyle factors. Details about the SEPAHAN project have been published elsewhere [12]. In brief, this study was performed among Iranian general adults working in 50 different health care centers affiliated with Isfahan University of Medical Sciences across Isfahan province. In this project, data were collected in two main phases between April and May 2010. To collect information about anthropometric indices and demographic and lifestyle factors, including dietary intakes and physical activity, self-administered questionnaires were distributed among 10 087 individuals in the first phase, with 8691 participants returning the completed questionnaires (response rate: 86.16%). In the second phase, data regarding GI health were collected (response rate: 64.6%). Finally, we were able to match 4763 questionnaires in the second phase with their corresponding questionnaires in phase 1. In the present study, we excluded individuals who had total daily energy intakes outside the range of 800 to 4200 kcal/d and those who had missing data on any relevant variable. Therefore, data from 3363 individuals for whom complete information about both dietary intake and IBS were available were included in the current analysis. All participants provided written informed consent forms. The study protocol was ethically approved by the Regional Bioethics Committee of Isfahan University of Medical Sciences.

Dietary intakes assessment

Dietary data were collected using a Willett-format dish-based 106-item semi-quantitative food frequency questionnaire (DS-FFQ) that was designed and validated specifically for Iranian adults. Detailed information about the design, foods included, and the validity of this questionnaire has been published elsewhere [13]. Briefly, the questionnaire contained five categories of foods and dishes:

1. mixed dishes (cooked or canned: 29 items);
2. grains (different types of bread, cakes, biscuits, and potato: 10 items);
3. dairy products (dairies, butter, and cream: 9 items);
4. fruits and vegetables (22 items); and
5. miscellaneous food items and beverages (including sweets, fast foods, nuts, desserts, and beverages: 36 items).

For each food item, a commonly consumed portion size was defined. Participants were asked to report their dietary intakes of foods and mixed dishes based on nine multiple-choice frequency response categories varying from "*never or less than once a month*" to "*12 or more times per day*." The frequency response categories for the food list varied from six to nine choices. For foods consumed infrequently, we omitted the high-frequency categories, whereas for common foods with a high consumption, the number of multiple-choice categories increased. Finally, to convert the food items into grams, we computed the amount of each portion size based on the booklet of "household measures" and then computed the amount of intake by considering the frequency of consumption of each food item. The validity of DS-FFQ was examined in a subgroup of 200 randomly selected participants of the SEPAHAN project. All participants in the validation study completed the DS-FFQ at study baseline and 6 mo later. During this validation study, participants provided three detailed dietary records that were used as the gold standard. As shown in earlier studies, it seems that this questionnaire provides reasonably valid measures of long-term dietary intakes.

Development of the FDII

To construct the FDII, we used information from a previous study on 486 Tehrani female teachers, in which foods and food groups contributing to systemic inflammation were reported [14]. In that study, systemic inflammation was examined by assessing serum high-sensitivity C-reactive protein (hs-CRP), interleukin (IL)-6, and tumor necrosis factor (TNF)-α concentrations. Foods and food groups loaded in the healthy dietary pattern of that study were considered anti-inflammatory and those loaded in the Western dietary pattern were considered proinflammatory. This was done because of the inverse association found between a healthy dietary pattern and inflammation and a positive association between the Western dietary pattern and inflammation in that study [14]. In the present study, we calculated mean daily intakes of 28 predefined food groups (12 anti-inflammatory including fruits, fruit juices, fish, poultry, cruciferous vegetables, yellow vegetables, green leafy vegetables, other vegetables, tomatoes, legumes, whole grains, and tea and 16 proinflammatory including processed meats, red meats, eggs, butter, dairy, coffee, potatoes, French fries, refined grains, pizza, snacks, mayonnaise, soft drinks, sweets and desserts, hydrogenated fats, and hydrogenated oils). First, we calculated energy-adjusted amounts of these food groups using a residual method [15]. Then, mean daily intakes were multiplied by their given factor loadings, obtained from our previous study [14], for each participant. The overall FDII score for each participant was then computed by summing the scores of each food and food group. Finally, the FDII score was divided by 100 to reduce the magnitude of the scores. Similar approaches were used in previous publications on the FDII.

Assessment of IBS

A modified Persian version of the Rome III questionnaire, as part of the main comprehensive questionnaire, was used for assessment of IBS. During the face validation of the questionnaire, we found that most participants were unable to distinguish between the descriptors used in the original Rome III questionnaire (*never, less than 1 d a month, 1 d a month, 2-3 d a month, 1 d a week, more than 1 d a week, every day*). Therefore, we modified the rating scales to consist of only four descriptors (i.e., *never or rarely, sometimes, often,* and *always*). We also decided to ask about the presence of each symptom in the previous 3 mo instead of questioning patients about the beginning of each symptom >6 mo before the evaluation, which already exists in original Rome III questionnaire. IBS was defined according to Rome III criteria as having recurrent abdominal pain or discomfort, at least sometimes, in the previous 3 mo associated with two or more of these criteria: improvement with defecation, at least sometimes, and onset associated with change in frequency or form (appearance) of stool, at least sometimes. IBS with constipation (IBS-C) was defined as having IBS and both of the following criteria: hard or lumpy stools at least sometimes and lack of loose, mushy, or watery stools. IBS with diarrhea (IBS-D) was defined as having IBS and both of the following criteria: lack of hard or lumpy stools and loose, mushy, or watery stools at least sometimes. Mixed IBS (IBS-M) was defined as having IBS and both of the following criteria: hard or lumpy stools at least sometimes and loose, mushy, or watery stools at least sometimes. The severity of IBS was examined by asking participants about the severity of their abdominal pain in the previous 3 mo. They were able to choose one of these responses: *mild, moderate, severe,* or *very severe.*

Assessment of other variables

Required information on other variables including age, sex, marital status, smoking status, medication use, and disease history (diabetes and colitis) was

Table 1
General characteristics of study participants across quintiles of the FDII score*

Quintiles of FDII score Variables	Q1	Q3	Q5	*P*-value†
Participants, n	672	672	672	
Age, y	37.8 ± 8.07	35.9 ± 7.6	35.1 ± 7.9	<0.001
BMI, kg/m^2	25.02 ± 3.8	24.8 ± 3.7	24.5 ± 3.7	0.005
Female, %	61.9	60.9	53.6	0.01
Married, %	80.3	80.2	81.1	0.45
Physically active, %	15	14.1	10.3	0.03
Current smokers, %	16.5	12.6	13.4	0.24
Disease history, %	3.4	2.8	3.4	0.79
Regular meal pattern, %				0.18
Often or always	63.9	59.5	60.4	
Never or occasionally	36.1	40.5	39.6	
Chewing sufficiency, %				0.14
A lot	13.8	11.1	12.7	
Not a lot	86.2	88.9	87.3	
Fluid consumption, %				0.63
<3 glasses	96.6	96.7	97.6	
≥3 glasses	3.4	3.3	2.4	
Tooth loss, %				0.18
Have all teeth	33.3	35.8	34.3	
Lost 1–5 teeth	57.3	58.3	59.4	
Lost >5 teeth	9.5	5.9	6.3	

FDII, empirically derived food-based dietary inflammatory index
*Data are mean ± SD.
†Obtained from analysis of variance or χ^2 test, where appropriate.

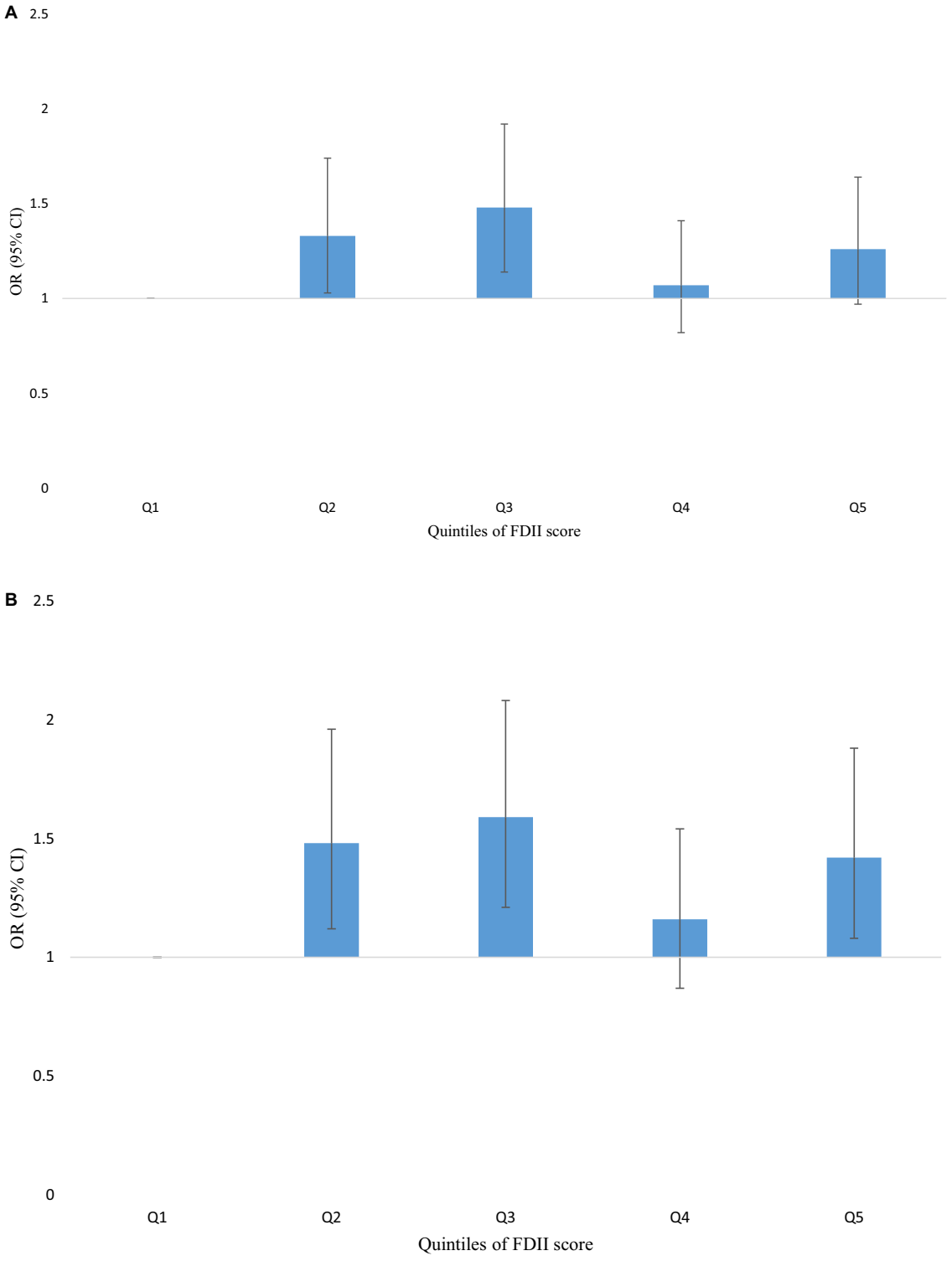

Fig. 1. (**A**) Association between the FDII score and IBS in the whole population (crude model). (**B**) Association between the FDII score and IBS in the whole population (multivariable-adjusted model). FDII, empirically derived food-based dietary inflammatory index; IBS, irritable bowel syndrome.

obtained from demographic and medical history questionnaires. Physical activity was assessed using the General Practice Physical Activity Questionnaire, and participants were classified into two categories: physically active (≥1 h/wk) and physically inactive (<1 h/wk). Although this level of activity might seem low, earlier publications revealed that even 1 h/wk of walking can reduce the risk for chronic conditions. Data on diet-related practices including meal regularity (often or always/never or occasionally), chewing efficiency (a lot/not a lot), and intra-meal fluid intake (<3 glasses/≥3 glasses) were also assessed through the use of a pretested questionnaire. Dental status was also examined and subjects were categorized as "having all teeth," "lost 1 to 5 teeth," and "lost >5 teeth." Anthropometric measures including weight, height, and waist circumference (WC) were assessed using a self-administered questionnaire. The validity of self-reported values of weight, height, and WC was examined in a pilot study with 200 participants from the same population. In the validation study, self-reported values of anthropometric indices were compared with actually measured values. The correlation coefficients for self-reported weight, height, and WC versus corresponding

measured values were 0.95 ($P < 0.001$), 0.83 ($P < 0.001$), and 0.60 ($P < 0.001$), respectively. BMI was calculated by dividing weight (kg) to height (m^2). The correlation coefficient for computed BMI from self-reported values and the one from measured values was 0.70 ($P < 0.001$).

Statistical anaysis

We classified participants based on quintile cutoff points of the FDII score. General characteristics of study participants across quintiles of the FDII score were presented as means ± SD for continuous variables and percentages for categorical variables. To examine the differences across quintiles, we used analysis of variance for continuous variables and χ^2 test for categorical variables. Energy-adjusted dietary intakes of study participants across quintiles of the FDII score were compared using analysis of covariance. We used binary logistic regression to estimate odds ratios (ORs) and 95% confidence intervals (CIs) for the presence of IBS and its subtypes across quintiles of the FDII score in the crude and multivariable-adjusted models. The trend of ORs across quintiles of the FDII score was determined by considering quintiles of the FDII score as ordinal variables in the logistic regression analysis. We also used multivariable ordinal logistic regression to estimate ORs and 95% CIs for assessing IBS severity (mild, moderate, severe, very severe) across quintiles of the FDII score in the crude and multivariable-adjusted models. In all these analyses, sex (male/female), smoking status (non-smoker/former smokers and current smokers), physical activity (<1 h/wk or ≥1 h/wk), medication use (yes/no), self-reported diabetes (yes/no) and colitis (yes/no), meal regularity (often or always/never or occasionally), chewing sufficiency (a lot/not a lot), intra-meal fluid consumption (<3 glasses or ≥3 glasses), and dental status (have all teeth, lost 1–5 teeth, or lost >5 teeth) were adjusted for in the multivariable-adjusted model. All statistical analyses were done using the SPSS version 20 (SPSS Inc., Chicago, IL, USA). $P < 0.05$ was considered as statistically significant.

Results

The FDII score ranged from −14.67 to +8.29 in this study. Median of the FDII score across increasing quintiles of FDII were −3.52, −1.53, −0.32, +0.75, and +2.46, respectively. In this study, 22.2% of participants were affected by IBS (n = 748). General characteristics of study participants are presented in Table 1. Compared with those in the lowest quintile, participants in the highest quintile of the FDII score were younger, less likely to be overweight, were women, and were physically active. No significant differences were observed in terms of other variables across quintiles of the FDII score.

A higher FDII score was significantly associated with higher intakes of dairy, refined grains, pizza, soft drinks, and hydrogenated oils and lower intakes of fruit, fruit juices, poultry, legumes, cruciferous vegetables, green leafy vegetables, yellow vegetables, other vegetables, tea, coffee, tomatoes, whole grains, red meats, processed meats, sweets and desserts, french fries, mayonnaise, and hydrogenated fats (data not shown).

In the crude model, there was no significant association between the FDII score and risk for IBS (OR, 1.26; 95% CI, 0.97–1.64) comparing extreme quintiles (Fig. 1A). However, in the multivariable-adjusted model, participants in the highest quintile of the FDII score had 42% greater chance for having IBS than those in the lowest quintile (OR, 1.42; 95% CI, 1.08–1.88) (Fig. 1B).

Sex- and BMI-stratified analyses on the association of the FDII and prevalence of IBS are shown in Table 2. When the analyses were done separately by sex, we found that there was no significant association between the FDII score and prevalence of IBS in men in neither the crude nor the adjusted model; however, among women we observed a significant association between the FDII score and IBS in the multivariable-adjusted model (OR, 1.44; 95% CI, 1.01–2.04), such that women in the top quintile of the FDII score were 1.44 times more likely to have IBS than women in the bottom quintile. By BMI status, normal weight individuals (BMI <25 kg/m^2) in the highest quintile of the FDII score had higher risk for IBS than those in the lowest quintile in the crude model (OR, 1.48; 95% CI, 1.01–2.16). This association remained significant even after further adjustment for potential confounders (OR, 1.60; 95% CI, 1.07–2.35). However, we failed to find any significant association between the FDII score and risk for IBS in overweight or obese individuals (BMI ≥25 kg/m^2) either before (OR, 1.10; 95% CI, 0.74–1.62) or after controlling for potential confounders (OR, 1.27; 95% CI, 0.84–1.94).

Table 2
Sex- and BMI-stratified ORs and 95% CIs for IBS across quintiles of the FDII score*

	Quintiles of FDII score			
Median FDII	Q1 −3.52	Q3 −0.32	Q5 +2.46	P_{trend}
Male				
Crude	1.00	1.32 (0.84–2.07)	1.25 (0.80–1.93)	0.98
Multivariable-adjusted†	1.00	1.53 (0.95–2.47)	1.40 (0.88–2.23)	0.70
Female				
Crude	1.00	1.59 (1.16–2.19)	1.33 (0.95–1.87)	0.19
Multivariable-adjusted†	1.00	1.62 (1.16–2.27)	1.44 (1.01–2.04)	0.16
BMI <25 kg/m^2				
Crude	1.00	1.84 (1.26–2.68)	1.48 (1.01–2.16)	0.13
Multivariable-adjusted‡	1.00	1.84 (1.24–2.71)	1.60 (1.07–2.35)	0.09
BMI ≥25 kg/m^2				
Crude	1.00	1.24 (0.85–1.81)	1.10 (0.74–1.62)	0.69
Multivariable-adjusted‡	1.00	1.38 (0.92–2.07)	1.27 (0.84–1.94)	0.83

BMI, body mass index; FDII, empirically derived food-based dietary inflammatory index.
*Values are OR (95% CIs).
†Adjusted for physical activity, smoking status, medication use, disease history (diabetes, colitis), regular meal pattern, chewing sufficiency, fluid consumption, and dental status.
‡Adjusted for sex, physical activity, smoking status, medication use, disease history (diabetes, colitis), regular meal pattern, chewing sufficiency, fluid consumption, and dental status.

Crude and multivariable-adjusted ORs and 95% CIs for the association of the FDII score and subtypes of IBS are provided in Table 3. There was no significant association between the FDII score and subtypes of IBS (OR and 95% CI for the highest versus the lowest quintile of FDII for IBS with constipation: 1.39, 0.87–2.08; IBS with diarrhea: 1.41, 0.83–2.39; mixed IBS: 1.44, 0.75–2.77; unsubtyped IBS: 1.17, 0.72–1.90).

Comparing extreme quintiles, no significant association was demonstrated between the FDII and IBS severity in crude (OR, 1.08; 95% CI, 0.65–1.79; Fig. 2A) or fully adjusted model (OR, 1.16; 95% CI, 0.66–1.99; Fig. 2B) in participants with IBS. This was also

Table 3
Crude and multivariable-adjusted ORs and 95% CIs for IBS subtypes across quintiles of the FDII score*

	Quintiles of FDII score			
Median FDII	Q1 −3.52	Q3 −0.32	Q5 +2.46	P_{trend}
IBS-C				
Crude	1.00	1.17 (0.77–1.78)	1.17 (0.77–1.78)	0.54
Multivariable-adjusted†	1.00	1.19 (0.76–1.85)	1.39 (0.87–2.08)	0.22
IBS-D				
Crude	1.00	1.14 (0.68–1.91)	1.29 (0.78–2.12)	0.45
Multivariable-adjusted†	1.00	1.28 (0.75–2.19)	1.41 (0.83–2.39)	0.40
IBS-M				
Crude	1.00	2.18 (1.19–3.99)	1.52 (0.80–2.88)	0.85
Multivariable-adjusted†	1.00	2.05 (1.11–3.77)	1.44 (0.75–2.77)	0.87
IBS-U				
Crude	1.00	1.48 (0.97–2.28)	1.08 (0.69–1.71)	0.92
Multivariable-adjusted†	1.00	1.61 (1.02–2.53)	1.17 (0.72–1.90)	0.88

FDII, empirically derived food-based dietary inflammatory index; IBS, irritable bowel syndrome; IBS-C, IBS with constipation; IBS-D, IBS with diarrhea; IBS-M, mixed IBS; IBS-U, unsubtyped IBS.
*Values are OR (95% CIs).
†Adjusted for sex, physical activity, smoking status, medication use, disease history (diabetes, colitis), regular meal pattern, chewing sufficiency, fluid consumption and dental status.

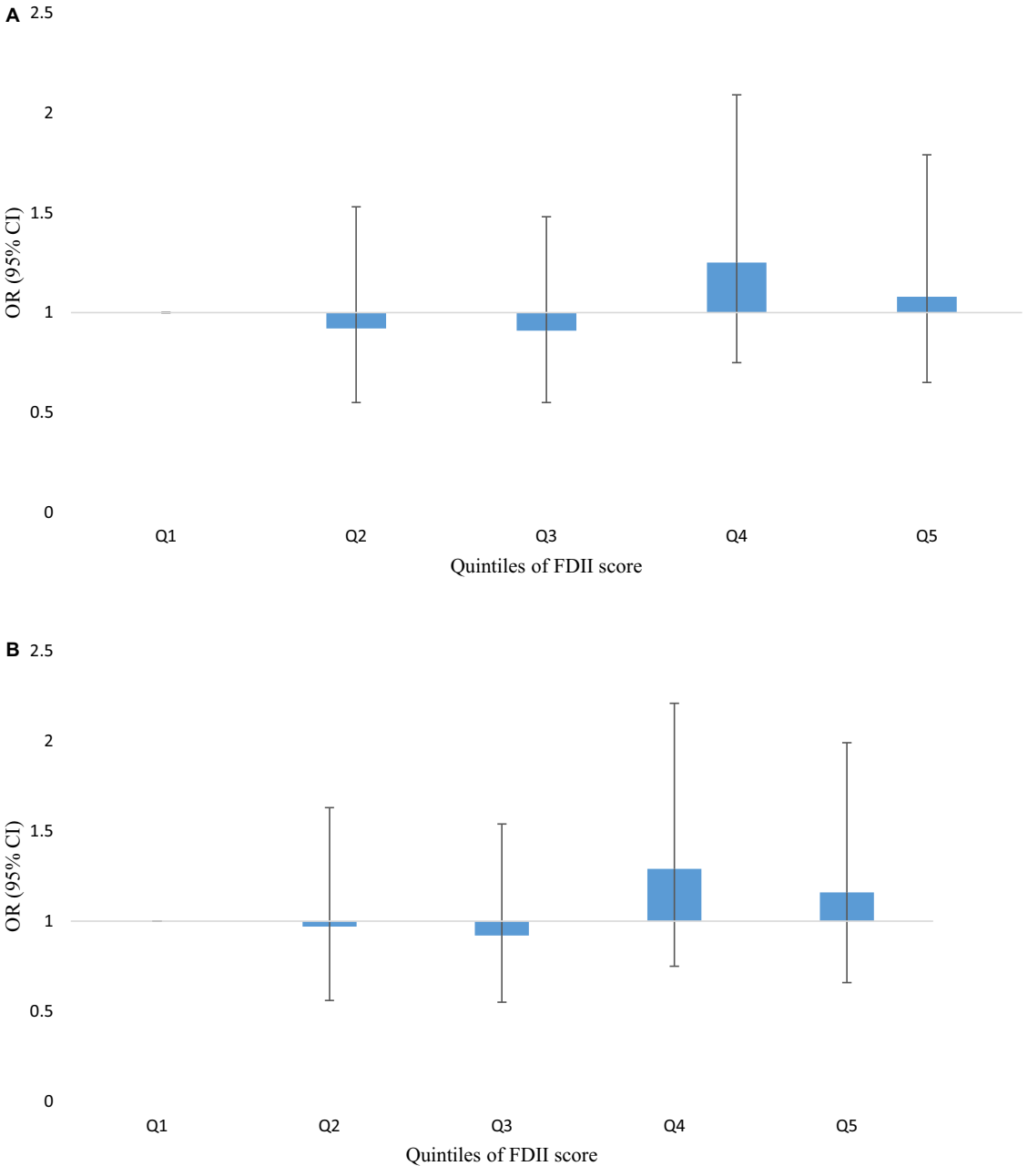

Fig. 2. (**A**) Association between the FDII score and IBS severity in the whole population (crude model). (**B**) Association between the FDII score and IBS severity in the whole population (multivariable-adjusted model). FDII, empirically derived food-based dietary inflammatory index; IBS, irritable bowel syndrome.

the case when we analyzed data separately by sex or BMI status (data not shown).

Discussion

Results from the present study found that consumption of a proinflammatory diet was associated with increased risk for IBS. We also observed a significant positive association between the FDII score and IBS among women, but not in men. In addition, a higher FDII score was associated with higher risk for IBS in normal weight (BMI <25 kg/m^2) individuals. No significant association was found between the FDII score and IBS severity. To our knowledge, this is the first study to examine empirically derived food-based DII in relation to IBS and its severity.

Lifestyle modification can be an effective strategy to improve quality of life in patients with IBS [16]. We found that consumption of a proinflammatory diet was associated with higher risk for IBS; however, there was no statistically significant association between the FDII score and IBS severity. To our knowledge, no previous study has examined the association of either food- or nutrient-based DII and the risk for IBS. However, it has been proposed that IBS is a proinflammatory condition [17]. Therefore, foods and nutrients that increase systemic inflammation probably contribute to the incidence or exacerbation of IBS symptoms. Based on these findings, adherence to a less proinflammatory diet should be recommended to prevent IBS.

In the present study, we found that women with a higher FDII score had higher risk for IBS; however, such associations were not

seen among men. The reasons for this observed sex discrepancy are not well understood; however, previous studies showed that IBS is more prevalent in women than in men [18]. The greater prevalence of IBS in women than men in the present study might also provide a reason for such finding. As is well known, proinflammatory foods and nutrients can increase serum levels of inflammatory cytokines such as hs-CRP and TNF-α [19]. These cytokines are mainly secreted from adipose tissue [20,21], which is higher in women than in men.

We observed a positive significant association between consumption of a proinflammatory diet and IBS in normal weight (BMI <25 kg/m^2), but not in overweight and obese (BMI ≥25 kg/m^2) individuals. As is well known, obesity is associated with increased levels of circulating inflammation [21]. It seems that obesity conceals the link between proinflammatory diet and IBS, which might be explained by excess fat deposition. Therefore, the inflammatory potential of the diet is more obvious in normal weight people than in overweight or obese individuals. Further studies are required to shed light on this issue.

The mechanisms through which a proinflammatory diet might contribute to IBS are not well understood. However, it seems that consumption of a proinflammatory diet can exacerbate IBS symptoms by increasing serum levels of inflammatory cytokines. A previous study showed that inflammatory cytokines affect nociceptor terminals and activate intracellular signaling pathways that can in turn increase peripheral and central nervous systems sensitivity resulting in pain hypersensitivity [7]. In addition, the role of gut microbiota in the pathophysiology of the FGIDs also has received much attention [22]. Gut microbiota contribute to immune mucosal hemostasis and maintenance of gut barrier structure and its function [23]. On the other hand, dietary intakes play a key role in the modulation of gut microbiota composition [24]. For instance, consumption of a high-fat diet promotes the development of a proinflammatory gut microbiota. In addition, the composition of gut microbiota among individuals who consumed Western diets were significantly different from those who consumed high-fiber diets [24]. Therefore, consumption of a proinflammatory diet might alter gut microbiota, which can affect GI health.

The present study had some strengths as well as limitations. First, this is the first study on the association of the FDII score to IBS and its severity. Second, we used empirically derived food-based DII to assess the inflammatory potential of the diet. In addition, this study included a large sample size and took a large number of confounders into account. Moreover, dietary habits that have been shown to play an important role in GI disorders were considered as covariates in this analysis. Some limitations should also be considered. First, owing to the cross-sectional nature of the present study, causal relationships could not be established. Therefore, further studies, especially with prospective designs, are needed in this area to confirm the present results. Second, although we controlled for several potential confounders, residual confounders could not be excluded. In the present study, we used a validated DS-FFQ for dietary assessment and development of the FDII score; however, measurement errors and misclassification of study participants in terms of exposure could not be avoided. In addition, for assessment of IBS, we used questionnaire-based data in this study. Although the validity of the Rome III questionnaire has been shown in Iranian adults, the possibility of misclassification of study participants in terms of outcome could not be avoided. We constructed the FDII based on factor loadings of food groups in healthy or Western dietary patterns among Iranian female teachers. In other words, measurement of inflammatory cytokines was not done in the present study population. This was also done in earlier publications about the FDII. However, it is recommended that the FDII be developed in the same population based on measurement of inflammatory cytokines. Although this might influence the findings, it is unlikely to distort the relations we found. Although overweight and obesity has been associated with a higher likelihood of developing IBS [25,26], surprisingly we found no significant association between consumption of a proinflammatory diet and IBS in individuals with a high BMI (≥25 kg/m^2). This might be attributed to the fact that most participants in the present study were young adults with normal weight and the study might not power enough to detect this association in overweight people. In addition, in our previous analysis on this population, we failed to observe any significant association between general or abdominal obesity and risk for IBS [27].

Conclusion

We found that adherence to a proinflammatory diet was associated with increased risk for IBS in the entire population, but in particular in women and those with normal BMI. No significant relationship was observed regarding the FDII score, IBS severity, and IBS subtypes.

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