



Dietary Inflammatory and Glycemic Indices in Newly Diagnosed Irritable Bowel Syndrome Patients Compared to Healthy People: A Case-Control Study

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ABSTRACT

Background: Limited studies have shown the possible relationship between dietary inflammatory potential and the risk of irritable bowel syndrome (IBS). However, no study has specifically assessed the influence of dietary glycemic indices on the risk of IBS. We aimed to investigate the association between dietary glycemic and inflammatory indices with the risk of IBS occurrence.

Methods: A total of 161 newly diagnosed IBS patients, identified according to the Rome IV criteria, and 163 healthy controls (aged ≥ 18 years) participated in the study. The dietary inflammatory index (DII), glycemic index (GI), and glycemic load (GL) were computed based on a 168-item food frequency questionnaire.

Results: After adjusting for baseline parameters, total DII showed a significant effect on the risk of IBS (OR = 0.41, 95% CI = 0.268, 0.62; $P < 0.001$). Participants in the last quartile of DII showed a 3.8-fold increased risk of IBS compared to those in the lowest quartile (95% CI = 1.92, 7.6; $p < 0.001$). In addition, a higher dietary total GL increased the risk of IBS by 52% (95% CI = 0.34-0.64, $p < 0.001$). Moreover, patients in the highest quartile of dietary GL showed a 21.7-fold greater risk of IBS compared to those in the lowest quartile ($p < 0.001$). An increase in lactose and fructose intake increased the risk of IBS by 10% ($p = 0.03$) and 13% ($p = 0.01$), respectively. Conversely, higher fiber intake decreased the risk of IBS by 11% ($p = 0.04$).

Conclusion: This study showed a possible positive association between diets characterized by high DII and GL and the risk of IBS.

1. Introduction

Irritable bowel syndrome (IBS) is the most common gastrointestinal (GI) disorder with different prevalence rates in the world. It is characterized by abdominal pain and changes in bowel habits, with three predominant subtypes: diarrhea-predominant, constipation-predominant, and mixed (Holtmann et al., 2016; Oka et al., 2020; Jahangiri et al., 2012; El-Salhy, 2012). The pathophysiology of IBS remains poorly understood, although multiple hypotheses have been proposed. A significant association has been identified between depression and IBS. Moreover, factors such as mucosal immune activation, inflammatory cells,

elevated inflammatory markers, and mutation in the genes responsible for these pathways have been proposed (Ng et al., 2018; Lee & Park, 2014; Kennedy et al., 2014). A genetic sequencing study involving 584 IBS patients and 1,380 asymptomatic controls showed functionally deleterious mutations in 2.2% of IBS patients. Specifically, loss-of-function and single nucleotide polymorphism were observed in the *SCN5A* gene among those with constipation-predominant IBS (Beyder et al., 2014). Although more than 60 candidate genes have been studied for IBS, these studies primarily derive from case-control analyses conducted on small sample sizes (Henström & D'Amato, 2016). Due to the unclear pathophysiology and the absence of definitive cures



or treatments for this disorder, patients often prefer to bring modifiable factors such as changes in diet. Certain food items can exacerbate the pain and lead to the recurrence of the disease. Consequently, dietary components including fermentable oligosaccharides, disaccharides, monosaccharides, and polyols (FODMAP) are omitted, with a low FODMAP diet suggested as a first-line treatment for these patients (De Palma & Bercik, 2022). Some patients examine gluten- and lactose-free diets to relieve symptoms (Lenhart et al., 2018). It is important to note that dietary modifications should be tailored to the specific subtype of IBS and the severity of symptoms. Considering the high carbohydrate content in FODMAP-rich foods, both the quantity and quality of carbohydrates may be important in this disorder. Furthermore, as IBS is characterized as an inflammatory disease, the role of inflammation in its pathogenesis is increasingly recognized (Huang et al., 2023). Therefore, a diet with anti-inflammatory properties with low glycemic index (GI) and load (GL) may play a main role in relieving the patient's symptoms. Based on a previous cross-sectional study, the consumption of a pro-inflammatory diet was associated with an increased risk of IBS, particularly among women, especially in overweight/obese participants (Salari-Moghaddam et al., 2019). Moreover, another study reported a positive dietary inflammatory index (DII) in patients with IBS compared to healthy people (Eslampour et al., 2021). The GI is defined as the area under the 2 h curve of postprandial glucose after the consumption of a food product containing 50 g of digestible carbohydrate and expressed as the ratio of the glycemic response to the same amount of reference carbohydrate from glucose or white wheat bread consumed by the same person (Venn & Green, 2007). Integrating the GI of the food with the amount of given carbohydrates in portion size is named the GL provides a more accurate picture of postprandial glycaemia (Brand-Miller et al., 2009). Higher dietary GI and GL are related to disorders including obesity, type 2 diabetes, cardiovascular diseases, and some cancers (Lange et al., 2022). Based on our literature review, no study has been conducted to investigate the association between dietary GI and GL with IBS. Besides, studies on the association between the DII and IBS have not distinguished among various sub-types of IBS and included all of them in their studies (Salari-Moghaddam et al., 2019; Eslampour et al., 2021). Considering the cultural differences and eating habits in various cities, it is necessary to carry out a study to investigate the dietary inflammatory and glycemic indices in patients with IBS compared to healthy people. The present study aimed to compare the scores of dietary inflammatory and glycemic indices between patients with constipation-predominant IBS and healthy people who are living in Zanjan City, and to assess their associations with the risk of IBS occurrence.

2. Materials and Methods

2.1 Participants and study design

In the present case-control study, we included 161 newly diagnosed patients with IBS-constipation dominant, aged

15-45 years, living in Zanjan City. Participants were diagnosed according to the ROME IV criteria by a gastroenterologist, and all had normal results from endoscopic examinations. Recruitment occurred from January to July 2023. The control group consisted of family members of the patients without any known diseases. To ensure that dietary habits were not similar, controls did not reside in the same household as the patients. Family members were selected to minimize the potential genetic influences on the disorder. Patients were matched based on body mass index (BMI), depression status, and smoking, as these factors are known to significantly impact IBS. Informed consent was gathered from all participants. Pregnant and lactating women, patients with any endocrine disorders including hypo/hyper thyroids, diabetes, malignancies, and patients with other GI disorders such as reflux, gastritis, etc. along with IBS, liver, and renal disorders were not included. Athletes and participants with psychiatric and physiological disorders such as depression, alcohol and drug abuse, and intake of supplements were excluded. Participants on a special diet were excluded, too. After dietary analysis, participants with calorie intake lower than 800 kcal or higher than 5000 kcal were excluded. The Ethics Committee of Zanjan University of Medical Sciences approved the present study.

2.2 Baseline characteristics

Baseline characteristics, including sex, age, educational level, job, family member, smoking, and marital status were recorded at the first visit. Anthropometric measurements, such as weight, height, and waist circumference, were taken by a standard and calibrated scale. Weight was measured without shoes and with minimal clothing, while height was assessed in a relaxed posture by a non-elastic meter on the wall, ensuring that the patient's shoulders, buttocks, heels, and back of the head were in contact with the wall, and the patient looked forward. The BMI was computed by weight (kg) to height (m)² ratio. Waist circumference was measured in a standing position, with a tape measure placed horizontally around the midpoint, just above the hip bones. Physical activity levels were recorded by a validated physical activity questionnaire (IPAQ). The depression status of patients was evaluated using the Beck questionnaire.

2.3 Dietary intake, DII, GI, and GL calculation

Dietary intake was determined by a validated 168-item food frequency questionnaire (FFQ) (Mirmiran et al., 2010) that contains common dietary intake during the past 12 months (number of daily, weekly, monthly, and annual). Data was inserted into the N4 software and converted to grams per day. The calculation of dietary GI and GL has been described previously (Liu et al., 2000). In calculating the DII score, a total of 45 diverse food parameters were identified as being related to the six inflammatory biomarkers. Each of the 45 different food parameters was allocated a "food parameter-specific inflammatory effect score" through a process of counting the number of studies reporting a pro-

inflammatory, anti-inflammatory, and no inflammatory effect on one or more of the six inflammatory markers, and weighting the scores by study design and size of the literature pool (Shivappa et al., 2014). To compute DII scores for the participants in this study, first, dietary data was linked to a global database comprising estimates from 11 diverse populations. This database provided mean intake values and standard deviations for each food parameter. Each individual's diet was then converted into a z-score by subtracting the "standard global mean" for each food parameter and dividing this value by the standard deviation. To minimize the risk of "right skewing", this z-score was then converted to a centered percentile score. To create a food parameter-specific DII score for an individual, the centered percentile score from each individual was multiplied by the food parameter-specific inflammatory effect score. In order to obtain the overall DII score for each participant in the study, all of the food parameter-specific DII scores were then summed (Shivappa et al., 2014). The overall DII score could be positive or negative. Higher positive DII scores indicate more pro-inflammatory diets and more negative scores denote more anti-inflammatory diets. The highest DII score for a pre-inflammatory diet is 7.98, while the highest score for an anti-inflammatory diet is -8.87. A total of 32 of the 45 possible dietary components were used for DII calculation based on the food frequency questionnaire. These parameters include total calories, carbohydrates, protein, total fat, cholesterol, saturated fatty acids, mono- and poly-unsaturated fatty acids, omega-3 and omega-6 fatty acids, trans fats, total fiber, thiamin, riboflavin, niacin, pyridoxine, folic acid, cobalamin, vitamin C, fat-soluble vitamins including A, D, E, and beta carotene. Minerals including iron, magnesium, selenium, and zinc were included in this compute. Moreover, intake of tea, caffeine, garlic, onion, turmeric, pepper, and ginger were also included. As regards the DII score was calculated per 1000 calories of food consumed we used the energy-standardized version of the world database to control for the influence of total energy intake. We used published GI values which have been collected in a database previously. Foods from the FFQ were matched to foods with reported GI values based on calorie and nutrient content, types of ingredients, and processing. For other foods, the GI was measured using standard methods. Dietary GI was calculated using the formula dietary GI = $\sum \text{foods } C \times F \times \text{GI} / \sum \text{foods } C \times F$ where C represents the grams of carbohydrate in a serving of food, F is the frequency of consumption of the food, and GI is the glycemic index using glucose as the reference. Dietary GL was calculated as dietary GL = $\sum \text{foods } C \times F \times \text{GI} / 100$ or equivalently the product of total carbohydrate and dietary GI expressed as a percentage. The nutrients, dietary GI, and dietary GL were energy-adjusted using the residuals method (Willett, 2012).

2.4 Sample size and Statistical analysis

The sample size was determined by the below formula based on the previous study (Mousavi et al., 2019).

$$n = \frac{(z_{1-\frac{\alpha}{2}} + z_{1-\beta})^2 (\sigma_1^2 + \sigma_2^2)}{d^2}$$

Data were analyzed using descriptive and analytical statistical tests using one variable and multivariable statistical tests by analytical SPSS software, version 22. The data normality was assessed using the Kolmogorov-Smirnov test. Data were distributed normally and the independent sample t-test and one-way ANOVA were used. The binary logistic regression model was used to adjust the effect of baseline parameters on the risk of IBS occurrence.

3. Results and Discussion

Table 1. Comparing participants in the newly diagnosed patients with irritable bowel syndrome with healthy one

Variables	Group	IBS (N = 161)	Healthy (N = 163)	p-value
Age, yr		35.2 ± 9.5	32 ± 9.5	0.002
BMI, kg/m ²		25 ± 2.8	24.8 ± 4.1	0.64
Waist circumference, cm		83.8 ± 6.4	85.4 ± 8.2	0.052
Sex				0.002
Male		35 (31.7%)	62 (38%)	
Female		126 (78.3%)	101 (62%)	
Marital status				< 0.001
Single		44 (27.3%)	77 (47.2%)	
Married		117 (72.7%)	86 (52.7%)	
Educational level				< 0.001
Illiterate		3 (1.9%)	-	
Primary		36 (22.4%)	6 (3.7%)	
Diploma		45 (28%)	24 (14.7%)	
University		77 (47.8%)	133 (81.6%)	
Family members 1-2				
3-4		26 (16.2%)	32 (19.9%)	0.032
5-6		96 (59.6%)	111 (68.1%)	
≥ 7		34 (21.1%)	13 (7.9%)	
		5 (3%)	8 (4.9%)	
Depression				
Mild		88 (54.7%)	96 (58.9%)	0.828
Moderate		55 (34.2%)	39 (23.9%)	
Sever		18 (11.2%)	28 (17.2%)	
Physical activity				
Mild		77 (47.8%)	81 (49.7%)	0.794
Moderate		64 (39.8%)	62 (38%)	
Sever		20 (12.4%)	20 (12.3%)	
Smoking				0.792
Yes		10 (6.2%)	9 (5.5%)	
No		151 (93.8%)	154 (94.5%)	
Job				0.006
Unemployed		114 (70.8%)	97 (59.5%)	
Self-employed		36 (22.4%)	39 (23.9%)	
Civil servant		11 (6.8%)	27 (16.6%)	
DII		-0.75 ± 1.9	-1.2 ± 1.8	0.05
GI		91.9 ± 48.9	72.8 ± 30.4	< 0.001
GL		37.8 ± 16.04	19.8 ± 11.9	< 0.001

*IBS; irritable bowel syndrome, BMI; body mass index, DII; dietary inflammatory index, GI; glycemic index, GL; glycemic load

*Quantitative variables were compared with the independent sample t-test and results have been presented as the means ± SD

*Qualitative variables were analyzed by the chi-square test and results have been presented as the number and percent

The baseline characteristics of patients with IBS compared to healthy people have been shown in Table 1. Age, weight, and height, but not BMI, had statistically significant differences between the two groups ($p = 0.002$, $p = 0.026$ and $p = 0.001$, respectively). In both groups, more participants were female with married status ($p = 0.002$ and $p < 0.001$, respectively). Educational level was significantly different between the two studied groups. More people in the healthy

group had a university education compared to the IBS group and less than half of patients carried university courses ($p < 0.001$). Most patients with IBS were unemployed, however, more people in the healthy group were civil servants and self-employed ($p = 0.006$). DII had a near-to-significant difference between the two groups. The inflammatory index of diet was significantly higher in the healthy group than in the patients with IBS ($p = 0.05$). Patients with IBS consumed a diet with higher GI and GL than healthy people ($p < 0.001$ and $p < 0.001$, respectively). Depression, physical activity level, and smoking status were not statistically significant between the two groups. As shown in Table 2, daily intake of energy, protein, carbohydrate, fiber, sucrose, and lactose were significantly different between the two groups. Patients in the IBS group consume higher sucrose ($p = 0.04$) per day than healthy people. In contrast, healthy people consumed more calories ($p = 0.001$), protein ($p < 0.001$), carbohydrate ($p < 0.001$), fiber ($p = 0.04$), and lactose ($p < 0.001$) per day compared to the patients with IBS. Moreover, patients with IBS consumed more caffeine per day than healthy people, however, this difference was near the significant level ($p = 0.06$). Significant variables including total carbohydrate, protein, fiber, sucrose, and lactose were adjusted based on the total calorie intake. Results showed that 71.9% and 64.5% of total calories were prepared from carbohydrates in the IBS and health groups, respectively which was statistically significant ($p = 0.002$). Moreover, lactose and sucrose intake were statistically significant between the two groups adjusted for total calories ($p < 0.001$ and $p < 0.001$, respectively).

Table 2. Dietary intake of calories and macronutrients in the studied groups

Groups Variables	IBS (N = 161) Means \pm SE	Healthy (N = 163) Means \pm SE	<i>p</i> -value*
Energy, kcal/d	2530.3 \pm 63.4	2907.7 \pm 63.4	0.001
Protein, g/d	85.77 \pm 2.9	103.1 \pm 3.89	< 0.001
Carbohydrate, g/d	344.6 \pm 8.7	419.2 \pm 14.4	< 0.001
Fat, g/d	95.2 \pm 3.3	97.3 \pm 2.9	0.621
Saturated fat, g/d	29.9 \pm 1.1	30.3 \pm 0.99	0.77
Mono-unsaturated fat, g/d	32 \pm 1.3	33.3 \pm 0.99	0.435
Poly-unsaturated fat, g/d	19.45 \pm 0.87	20.04 \pm 0.68	0.593
Trans fat, g/d	0.0005 \pm 0.0002	0.0007 \pm 0.0002	0.4
Fiber, g/d	50 \pm 2	55 \pm 2.3	0.041
Sucrose, g/d	26.96 \pm 1.43	23.3 \pm 1.4	0.041
Lactose, g/d	8.8 \pm 0.56	14.1 \pm 0.84	< 0.001
Fructose, g/d	18.87 \pm 0.65	21.12 \pm 1.07	0.071
Caffeine, mg/d	141.4 \pm 9.4	121.6 \pm 6.7	0.061

*analyzed by independent sample t-test

Dietary GI and GL, as well as DII in the various quartiles, are presented in Table 3. Participants in the first quartile of DII had more negative DII than the others. The 4th quartile of DII in the IBS patients was significantly more positive than the healthy group ($p < 0.001$). In addition, DII in the 3rd quartile was significantly more negative than the same in the patients with IBS ($p = 0.002$). Dietary GI was significantly higher in the first and 3rd quartile of patients with IBS than in the healthy group ($p < 0.001$ in both). Moreover, the number of participants in the first quartile of dietary GI was significantly higher in the healthy group than in the patients with IBS ($p < 0.001$). However, more patients with IBS

received a diet with high GI, dietary GL showed no significant difference between the quartiles in patients with IBS compared to the healthy group.

Table 3. Dietary inflammatory and glycemic indices in the various quartiles of the studied groups

Groups	Quartile	DII (N) Means \pm SD	GI Means \pm SD	GL Means \pm SD
IBS	1	-3.1 \pm 0.65 (40)	50.8 \pm 22.4 (23)	20.5 \pm 11.7 (40)
	2	-1.5 \pm 0.39 (40)	123.05 \pm 22.8 (40)	60.5 \pm 11.6 (40)
	3	-0.12 \pm 0.4 (41)	208.5 \pm 24.1 (42)	101 \pm 11.98 (41)
	4	1.68 \pm 0.95 (40)	285.8 \pm 24.8 (56)	141.5 \pm 11.7 (40)
<i>p</i> -value		< 0.001	< 0.001	< 0.001
Healthy	1	-3.5 \pm 0.79 (40)	37.1 \pm 22.9 (58)	20.5 \pm 11.7 (40)
	2	-1.9 \pm 0.36 (41)	120.9 \pm 24.5 (41)	61 \pm 11.97 (41)
	3	-0.67 \pm 0.35 (41)	197.1 \pm 21.7 (39)	102 \pm 11.9 (41)
	4	1.3 \pm 1.07 (41)	280 \pm 20.07 (25)	143 \pm 11.9 (41)
<i>p</i> value ^a		< 0.001	< 0.001	< 0.001

*IBS: irritable bowel syndrome; DII: dietary inflammatory index; GI: glycemic index; GL: glycemic load

† Compared based on ANOVA test

Mean differences and standard error of DII, GI, and GL among various quartiles are shown in Table 4. As shown in the IBS and healthy groups, there was a significant difference among various quartiles of DII, dietary GI, and GL ($p < 0.001$). After adjusting for baseline parameters, including sex, age, weight, height, waist circumference, job, family member, educational level, marital status, energy, and macronutrient intake, the DII of patients with IBS was significantly different compared to the healthy people (OR = -0.14, 95% CI = -0.98, -0.048; $p = 0.03$). To adjust the effects of significant variables on the risk of IBS, a binary logistic regression model was used. The total DII showed a significant effect on IBS (OR = 0.41, 95% CI = 0.268, 0.62; $P < 0.001$). Participants in the highest quartile of DII showed a 3.8-fold higher risk for IBS than those in the lowest quartile (95% CI = 1.92, 7.6; $p < 0.001$). Moreover, a higher dietary total GL increased the risk of IBS by 52% (95% CI = 0.34-0.64, $p < 0.001$). Participants in the highest quartile of dietary GL showed a 21.7-fold increased risk of IBS than participants in the lowest quartile ($p < 0.001$). In contrast, dietary total GI and its quartiles had no significant effect on the risk of IBS. This may be related to the fact that GL accounts for both the quantity and quality of carbohydrates, while GI focuses only on the glycemic response. Consequently, dietary GL is considered more applicable and accurate than GI. On the other hand, increases in lactose and fructose intake increased the risk of IBS by 10% ($p = 0.03$) and 13% ($p = 0.01$), respectively. Higher fiber intake decreased the risk of IBS by 11% ($p = 0.04$). An increase in daily carbohydrate intake increased the risk of IBS by 1.01-fold (95% CI = 1.007-1.024, $p < 0.001$). Marital status also showed a significant effect on the risk of IBS, with single participants having a 4.59-fold higher risk for IBS occurrence (95% CI = 1.35-15.63, $p = 0.01$) (Table 5).

Table 4. Mean differences in dietary inflammation, glycemic index, and load among the quartiles of the studied groups

Groups	Dietary index		Quartile		Mean difference	Standard error	<i>p</i> value†	95% Confidence interval
Dietary Inflammatory index								
IBS	1	2	3	-1.65	0.14	< 0.001	-2.02, -1.27	
				-2.9	0.14	< 0.001	-3.36, -2.6	
				-4.8	0.14	< 0.001	-5.2, -4.4	
	2	1	3	1.65	0.14	< 0.001	1.2, 2.02	
				-1.33	0.14	< 0.001	-1.7, -0.97	
				-3.14	0.14	< 0.001	-3.5, -2.8	
	3	1	2	2.98	0.14	< 0.001	2.62, 3.35	
				1.34	0.14	< 0.001	0.97, 1.7	
				-1.8	0.14	< 0.001	-2.1, -1.4	
	4	1	2	4.79	0.14	< 0.001	4.4, 5.2	
				3.1	0.14	< 0.001	2.77, 3.5	
				1.8	0.14	< 0.001	1.43, 2.2	
Healthy	1	2	3	-1.6	0.16	< 0.001	-2.01, -1.2	
				-2.8	0.16	< 0.001	-3.2, -2.4	
				-4.8	0.16	< 0.001	-5.2, -4.4	
	2	1	3	1.6	0.16	< 0.001	1.2, 2.01	
				-1.2	0.16	< 0.001	-1.6, -0.8	
				-3.2	0.16	< 0.001	-3.6, -2.8	
	3	1	2	2.81	0.16	< 0.001	2.4, 3.2	
				1.2	0.16	< 0.001	0.8, 1.6	
				-2.01	0.16	< 0.001	-2.4, -1.6	
	4	1	2	4.8	0.16	< 0.001	4.4, 5.2	
				3.2	0.16	< 0.001	2.8, 3.6	
				2.01	0.16	< 0.001	1.6, 2.4	
Dietary Glycemic index								
IBS	1	2	3	-72.2	6.23	< 0.001	-88.4, -56.3	
				-157.6	6.16	< 0.001	-173.7, -141.6	
				-234.95	5.9	< 0.001	-250.3, -219.6	
	2	1	3	72.2	6.2	< 0.001	56.02, 88.4	
				-85.4	5.3	< 0.001	-99.1, -71.75	
				-162.7	4.9	< 0.001	-175.5, 149.9	
	3	1	2	157.6	6.2	< 0.001	141.6, 173.7	
				85.4	5.2	< 0.001	71.7, 99.1	
				-77.3	4.8	< 0.001	-89.9, -64.7	
	4	1	2	234.9	5.9	< 0.001	219.6, 250.3	
				162.7	4.9	< 0.001	149.9, 175.5	
				77.3	4.8	< 0.001	64.7, 89.9	
Healthy	1	2	3	-83.9	4.62	< 0.001	-95.87, -71.9	
				-159.9	4.68	< 0.001	-172.1, -147.8	
				-242.9	5.4	< 0.001	-256.9, -228.8	
	2	1	3	83.87	4.6	< 0.001	71.8, 95.8	
				-76.1	5.06	< 0.001	-89.3, -62.9	
				-159.02	5.7	< 0.001	-173.9, -144.1	
	3	1	2	159.9	4.68	< 0.001	147.8, 172.2	
				76.1	5.06	< 0.001	62.9, 89.3	
				-82.9	5.8	< 0.001	-97.9, -67.8	
	4	1	2	242.9	5.4	< 0.001	228.8, 256.9	
				159.02	5.7	< 0.001	144.1, 173.9	
				82.9	5.8	< 0.001	67.8, 97.9	
Dietary glycemic load								
IBS	1	2	3	-40	2.63	< 0.001	-46.3, -33.2	
				-80	2.61	< 0.001	-87.3, -73.7	
				-121	2.63	< 0.001	-127.8, 114.2	
	2	1	3	40	2.6	< 0.001	33.2, 46.8	
				-40	2.61	< 0.001	-47.3, -33.7	
				-81	2.63	< 0.001	-87.8, -74.2	
	3	1	2	80	2.61	< 0.001	73.7, 87.3	
				40	2.61	< 0.001	33.7, 47.3	
				-40	2.61	< 0.001	-47.3, -33.7	
	4	1	2	121	2.63	< 0.001	114.2, 127.8	
				81	2.63	< 0.001	74.1, 87.8	
				40.5	2.61	< 0.001	33.7, 47.3	
Healthy	1	2	3	-40	2.64	< 0.001	-47.4, -33.6	
				-81	2.64	< 0.001	-88.4, -74.6	
				-122.5	2.64	< 0.001	-129.4, -115.6	
	2	1	3	40.5	2.65	< 0.001	33.6, 47.4	
				-41	2.63	< 0.001	-47.83, -34.2	
				-82	2.63	< 0.001	-88.8, -75.2	
	3	1	2	81	2.65	< 0.001	74.6, 88.4	
				41	2.63	< 0.001	34.2, 47.8	
				-41	2.63	< 0.001	-47.8, -34.2	
	4	1	2	122.5	2.64	< 0.001	115.6, 129.4	
				82	2.63	< 0.001	75.2, 88.8	
				41	2.63	< 0.001	34.1, 47.83	

†Assessed by the Tukey test following one-way ANOVA analysis

Table 5. Effect of total dietary inflammatory and glycemic indices and their quartiles on the risk of IBS

Variable	B	SE	Exp (beta)	95% CI	<i>p</i> value†	
sex	-0.13	0.45	0.87	0.363	2.11	0.768
age	-0.032	0.021	0.97	0.93	1.01	0.131
Marital status	1.52	0.62	4.59	1.35	15.63	0.01
Educational level	0.22	0.38	1.25	0.58	2.67	0.57
Family member	-0.083	0.11	0.92	0.744	1.14	0.44
Weight	-0.003	0.02	0.1	0.955	1.04	0.874
Height	0.007	0.023	1.01	0.962	1.05	0.758
Waist circumference	0.094	0.04	1.1	0.982	1.01	1.2
Job	0.286	0.211	1.33	0.87	2.01	0.176
Energy	0.000	0.001	1	0.99	1.002	0.56
Protein	-0.011	0.009	0.99	0.97	1.007	0.22
Carbohydrate	0.015	0.004	1.01	1.007	1.024	< 0.001
Fiber	-0.06	0.03	0.94	0.89	0.99	0.04
Sucrose	-0.011	0.02	0.99	0.95	1.03	0.56
Fructose	0.074	0.03	0.93	0.87	0.99	0.01
Lactose	0.06	0.03	1.1	1.005	1.12	0.03
Caffeine	0.001	0.002	1.001	0.99	1.004	0.67
Total DII	-1.28	0.26	0.28	0.2	0.45	< 0.001
Quartile of DII	1.7	0.42	5.5	2.4	12.5	< 0.001
Total GI	0.013	0.02	1.013	0.97	1.06	0.56
Total GL	-0.73	0.14	0.48	0.34	0.64	< 0.001
Quartile of GI	0.02	0.64	1.4	0.33	6.1	0.96
Quartile of GL	7.7	1.6	21.7	99.7	472.5	< 0.001

†The binary logistic regression model was used. DII: dietary inflammatory index; GI: Glycemic index; GL: glycemic loa

According to our literature review, there are limited studies on the association between DII and risk of IBS (Salari-Moghaddam et al., 2019). However, there is no study to assess the association of dietary GI and GL with the risk of IBS in constipation-dominant patients. Considering differences in dietary habits, type and amount of food intake, religious, environmental factors, and stressors among various countries, it is necessary to conduct localized studies that explore dietary intake and its relationship with prevalent diseases such as IBS, a common gastrointestinal disorder for which no definitive therapy exists. Previous studies have focused on dietary changes to relieve symptoms and resulted in inconclusive results (Salari-Moghaddam et al., 2019; Tigchelaar et al., 2017; Sinagra et al., 2016). One of the weaknesses of the existing research is the inclusion of all IBS subtypes within the participant pool, which complicates the interpretation of findings. The exact mechanism and pathophysiology of IBS remain inadequately understood; however, evidence suggests that low-grade chronic inflammation may play a role in the onset or exacerbation of IBS symptoms (de Graaf et al., 2022). A recent case-control study involving 155 IBS patients from Lorestan province in Iran reported a significantly higher mean DII score in IBS patients compared to healthy controls (0.78 ± 2.22 vs. -0.39 ± 2.27) (Eslampour et al., 2021). In this study, subjects in the fourth quartile had a 3.65-fold higher risk of IBS compared to those in the first quartile in the crude model. After adjusting for age and sex as covariates, the risk increased to 5.66-fold. These findings are in accordance with our results; however, it is important to note that the IBS participants in the mentioned study included those with diarrhea-predominant, constipation-predominant, and mixed-dominant subtypes. In our study, the total DII showed a significant effect on IBS and increased its risk by 59%. Similarly, participants in the highest quartile of DII showed a 3.8-fold higher risk of IBS compared to those in the lowest quartile. In the present study, only constipation-dominant IBS patients were recruited. Certainly, food choices and preferences are different in diarrhea-dominant with constipation-dominant patients. In addition, the mean DII score was negative in the patients with IBS and healthy groups (-0.75 ± 1.9 vs. -1.2 ± 1.8), but the DII score was more negative in the healthy group than the patients that showed the low inflammatory potential of the diet that received by healthy people compared with the IBS patients. A higher DII score that is more positive indicates a more pro-inflammatory diet and a lower DII score that is more negative indicates a more anti-inflammatory diet. In another case-control study, diet quality was compared in IBS patients with healthy controls by the Dutch Healthy Diet-Index 2015 (DHD-2015) and its inflammatory potential by the Adapted Dietary Inflammatory Index (ADII). Results showed that the DHD-2015 was significantly lower in the IBS than in controls. Moreover, DHD-2015 was significantly associated with abdominal pain ($b = -0.012$) and reflux syndrome ($b = -0.016$) in the IBS group. The ADII score showed no significant correlation with IBS (Shivappa et al., 2014). We didn't find a study on the correlation of dietary GI and GL with IBS risk in

constipation-dominant patients. As we know, constipated patients traditionally consume more fruits and fiber in their diet which increases their dietary glycemic load. A recent study on the IBS patient's adherence to Mediterranean diet (MD) with the severity of symptoms showed that the MD Adherence Screener scores were similar between IBS and healthy subjects and did not correlate with severity of IBS-Scoring System, abdominal pain, or bloating. Interestingly, IBS participants had a higher consumption of fruits, vegetables, sugar, and butter which was correlated with a greater severity of IBS symptoms (Chen et al., 2024). In the present study, healthy people consumed more carbohydrates and fiber in their diet compared to the IBS patients. However, sucrose consumption was significantly higher in the IBS group than the healthy people that makes higher osmolality in the gut and aggravates the disease. Moreover, in the adjusted model total carbohydrate, fiber, fructose, and lactose intake showed a significant effect on the IBS risk in patients who are constipation-dominant. Recently, there has been a lot of attention to the dietary glycemic index and load and the possible health benefits of including foods ranked low on the glycemic index in the diet because break down slowly, causing a steady release of glucose into the bloodstream (Sangal & Sangal, 2006). The beneficial effect of a low GI diet on some diseases including obesity diabetes, heart disease, gastric cancers, and breast and colorectal cancers is established (Foster-Powell et al., 2002; Willett, 2012). However, the interconnection between dietary GI and GL with IBS is under challenge (Mousavi et al., 2019). Our results showed no significant effect of dietary GI on IBS risk. However, dietary GL and its quartile showed a significant effect so the last quartile of dietary GL increased the risk of IBS by 21.7-folds. The GI is the postprandial glucose after the consumption of a food product containing 50 g of digestible carbohydrate compared to the reference carbohydrate, however, GL is an integrated form of dietary GI with the amount of given carbohydrates in a portion size that provides a more accurate picture of the postprandial glycaemia (Brand-Miller et al., 2009; Venn & Green, 2007). Therefore, focusing on dietary GL in diet therapy meetings is more valuable and applicable than the GI of foods. One of the advantages of the present study is that it was performed in one subtype of IBS (constipation-dominant). In addition, the effect of dietary GI and GL was studied for the first time in IBS patients. There are some limitations to the present study. The case-control design makes it difficult to reach a causal relationship between the exposure and outcome. Moreover, we didn't study the patient's symptoms and severity of disease to assess the correlation between DII, GI, and GL with symptoms including pain, bloating, and severity of constipation. Due to scarce studies in this field, there is a need to conduct more studies in various populations to reach a concise result.

4. Conclusion

IBS includes many clients to gastroenterologists with no clear pathophysiology or therapeutic role. However, studies

on the effects of different aspects of diet are not clear in this disorder and only a FODMAP diet, that is low in fermentable oligosaccharides, disaccharides, monosaccharides, and polyols, is suggested. Intake of a diet with high pro-inflammatory properties and glycemic load predisposes people to IBS occurrence. In conclusion, total DII and GL, along with their quartiles, demonstrate a significant effect on the risk of IBS in the Iranian population living in Zanjan City, located in the northwest of Iran. These results are applicable in dietary consulting meetings by dietitians. However, further research in different regions is necessary to attain more definitive conclusions.

Authors' Contributions

Seyedeh Neda Mousavi: Conceptualization; Project administration; Supervision; Visualization; Methodology; Validation; Writing-review & editing; Writing-original draft. Maryam Jameshorani: Conceptualization; Project administration; Supervision; Visualization; Methodology; Validation; Writing-review & editing. Kimia Shahbazi, Amir Mahmoodkhani: Data curation; Formal analysis; Writing-review & editing.

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Conflicts of Interest

All the authors report no relevant conflicts of interest for this article.

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Ethical considerations

This study was approved by the ethics committee of Zanjan University of Medical Sciences (Ethics no. IR.ZUMS.REC.1401.199).

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