



## Association of the Mediterranean-DASH Intervention for Neurodegenerative Delay Diet with Irritable Bowel Syndrome: A Multicenter Case Control Study

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### ABSTRACT

**Background:** The association between Mediterranean-DASH diet Intervention for Neurodegenerative Delay (MIND) diet score and irritable bowel syndrome (IBS) has been rarely investigated; therefore, the authors aim to investigate the association between MIND diet score and IBS odds. **Methods:** This case-control study was conducted on 876 adult participants. Dietary intake was evaluated using a validated 168-item food frequency questionnaire (FFQ). The MIND diet score was calculated using FFQ. Furthermore, socio-economic status, anthropometric measures, and blood pressure were recorded by a trained interviewer, using standard methods. Finally, logistic regression was used to investigate the association between MIND diet and IBS. **Results:** The mean age of the participants was 30.9 years. Being the last quantile of MIND diet score was associated with 19% lower odds of IBS in crude model. Also, a significant association was seen in the fully adjusted model; such that individuals in the top category of MIND diet score were 27% less likely to have IBS compared with those in the bottom category. **Conclusions:** In summary, the authors presented evidence showing a negative association between adherence to the MIND diet and odds of IBS. Ultimately, because of the likely preventive influence of diet, it is essential to elucidate the relationship between diet and IBS via extensive prospective cohort studies in the future.

### Introduction

Irritable bowel syndrome (IBS) is a common gastrointestinal (GI) disorder, marked by abdominal pain or discomfort and changes in bowel habits (Longstreth *et al.*, 2006). The global prevalence of IBS was 11.2 % (Lovell and Ford, 2012). This disorder is more prevalent among

females (Jahangiri *et al.*, 2012). The pathophysiology behind this disorder is intricate and not fully comprehended. Several possible factors, including dysfunction of the gut-brain axis, visceral hypersensitivity, alterations in GI motility and secretion, along with psychosocial influences,

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may elucidate its pathophysiology (Ohman and Simrén, 2007). This condition can lead to significant healthcare expenses and diminish the quality of life for these individuals (Dean *et al.*, 2005, Hillilä *et al.*, 2010, Paré *et al.*, 2006, Simrén *et al.*, 2006).

Lifestyle components such as diet have been shown to affect IBS symptoms (Böhn *et al.*, 2013, Hayes *et al.*, 2014). Past studies have reported that diets low in fermentable oligosaccharides, disaccharides, monosaccharides, and polyols (FODMAPs) could reduce the IBS symptoms (Halmos *et al.*, 2014, Nanayakkara *et al.*, 2016). Also, adherence to healthy dietary pattern was related to reduction in IBS odds (Khayyatadeh *et al.*, 2016). Another finding indicated that adherence to Mediterranean diet could be associated with decreased functional GI symptoms (Zito *et al.*, 2016). Because inflammation plays an important role in the pathophysiology of IBS, diets with anti-inflammatory potential such as Dietary approaches to stop hypertension (DASH) diet (Soltani *et al.*, 2018) may diminish some GI symptoms (Soltani *et al.*, 2021).

Considering the significant impact of mental health on IBS, dietary elements that influence psychological well-being might also affect IBS symptoms (Elsenbruch, 2011). Recently, the MIND diet (Mediterranean-DASH Diet Intervention for Neurodegenerative Delay) has been suggested as a diet that offers neuroprotective benefits and positive effects on mental health (Morris *et al.*, 2015). Like the Mediterranean and DASH diets, the MIND diet focuses on whole plant-based foods while restricting the consumption of animal products and foods that are high in saturated fats (Morris *et al.*, 2015). Research indicates that following the MIND diet is linked to a reduced likelihood of psychological disorders (Salari-Moghaddam *et al.*, 2019, van den Brink *et al.*, 2019). In addition, MIND diet is rich in polyphenols, which may help decrease inflammation (Roudsari *et al.*, 2019).

There is not enough evidence regarding the association between adherence to MIND diet and IBS odds. To the authors' knowledge, only one

cross-sectional study was conducted which indicated no significant relationship between adherence to the MIND diet and odds of IBS neither in the whole population nor in subgroup analysis (Nouri-Majd *et al.*, 2022). Since the IBS diagnosis in this research relied on questionnaires rather than precise medical evaluations, the misclassification of participants cannot be overlooked. The aim of this research was, consequently, to explore the relationship between following the MIND diet and the odds of IBS among a substantial group of Iranian adults.

## Materials and Methods

### *Study design and participant enrollment*

This multicenter case-control study was conducted in the years 2021 to 2023 in Lorestan University of Medical Sciences (city of Khorramabad), Urmia University of Medical Sciences and Kermanshah University of Medical Sciences. In this study, IBS patients of 18 to 60 from each center, who were referred to the specialized clinics of the mentioned universities, were selected based on the Rome III diagnostic criteria and with the approval of the gastroenterology subspecialist using the available sampling method. Patients with underlying diseases such as diabetes, liver and kidney dysfunction, cardiovascular disease, cancer; coeliac disease; inflammatory bowel disease and other digestive disorders; abdominal surgery; pregnancy; breastfeeding; having special diets, smoking, and alcohol consumption were excluded from the study. Patients who had used medication for the treatment of IBS were considered to meet the exclusion criteria. The type and the dose of medication used by IBS patients were variables whose effects were adjusted in statistical analyses.

In the same way, healthy people with no affliction of IBS or the aforementioned exclusion criteria were selected from the companions of other patients as a control group (the ratio of case to control samples was 1:2).

### *Anthropometric measurements*

Anthropometric measurements including height and weight were measured using stadiometer with

an accuracy of 0.1 cm and a digital scale with an accuracy of 100 grams. The body mass index (BMI) was calculated by dividing the body weight (kg) by the height ( $m^2$ ). (Ramstrand *et al.*, 2011).

#### **Dietary intake and analysis**

The dietary intake was assessed using the previously validated and reliable 168-item Food Frequency Questionnaire (FFQ) (Mirmiran *et al.*, 2010). In this questionnaire, there is a standard size for each food item, which is designed according to the Willet method.

First, during the face-to-face interview, the average size of each food item was explained, and then people were asked to report the frequency of consumption of each food item over the past year. Depending on the type of food consumed, the frequency of consumption per day, week, or month was asked. The amounts reported by the subjects for each food item were converted to grams per day using the home comparison guide book (Ghaffarpour *et al.*, 1999), and finally, the exact amounts of energy, micronutrients, and macronutrients consumed by each participant were calculated using the Nutritionist IV (N4) software.

#### **Severity of IBS symptoms**

The valid and reliable Extra-Intestinal Symptoms Severity Scale (EISSS) was used to assess the severity of extra-intestinal IBS symptoms (Nemati *et al.*, 2010). This instrument consists of 15 seven-item questions (from never to always) that assess non-intestinal symptoms associated with IBS, including vomiting and nausea, early satiety, headache, back pain, fatigue, excessive flatulence, checking for excess, heartburn, urgency to defecate, feeling of incomplete bowel movement, urgency to urinate, thigh pain, muscle or joint pain, feeling full after eating. The alternatives of sometimes to always experiencing the feeling were considered as the presence of a sign (Gholamrezaei *et al.*, 2011).

#### **Physical activity level**

The physical activity of the participants was assessed using the Iranian version of International

Physical Activity Questionnaire (IPAQ) (Moghaddam *et al.*, 2012). This questionnaire collected information about physical activity during working hours, commuting, household chores, and free time during the past 7 days. Then, according to the standard instructions, the total metabolic equivalent score (MetS) was calculated, and the participants were classified into groups of low (up to 600 met/min/week), moderate (600 to < 3000 met/min/week), and high (at least 3000 met/min/week) activity levels (Wareham *et al.*, 2003).

#### **MIND diet assessment**

Dietary intake was assessed through a face-to-face interview utilizing a 168-item semi-quantitative FFQ, which has already been validated and shown to be reliable in Iran (Mirmiran *et al.*, 2010). In this study, certain dietary components from the FFQ, shown in **Table 1**, were used to calculate the MIND diet scores. Out of the 15 dietary components in the initial scoring system of the MIND diet, 10 were categorized as beneficial for brain health (green leafy vegetables, other vegetables, nuts, berries, beans, whole grains, fish, poultry, olive oil, and wine), while 5 were identified as harmful (red meats, butter and stick margarine, cheese, pastries, and sweets, and fried/fast food). In this study, the authors employed a modified MIND diet scoring system tailored to Iranian dietary habits. In this scoring system, wine consumption was excluded (drinking was not allowed). The MIND scoring was applied to the other 14 food groups. Participants were then classified into tertile categories based on their dietary intake. Participants in the lowest third of brain-healthy food groups received a score of 0, those in the middle third were assigned a score of 0.5, and individuals in the highest third were given a score of 1. Conversely, the authors evaluated unhealthy food groups for brain health oppositely. The overall score was then calculated by adding together all the scores for the dietary components. Finally, the participants received a MIND diet score that varied from 0 to 14.

**Table 1.** Components of the MIND diet score.

<b>Brain-healthy foods score</b>		
1	Green leafy vegetables	Lettuce and greens
2	Other vegetables	Cucumber, tomatoes, tomato sauce, carrot, green beans, onion, potatoes, capsicum, peas, eggplant, cabbage, and mushrooms
3	Berries	Strawberries and berries
4	Nuts	Walnuts, pistachios, hazelnuts, almonds, peanuts, and seeds
5	Whole grains	Whole grains
6	Fish	Fish
7	Beans	Lentils, beans, chickpea, mung bean, and cotyledon
8	Poultry	Chicken
9	Olive oil	Olive oil
<b>Brain-unhealthy foods</b>		
10	Butter and margarine	Butter, cream, and hydrogenated fats
11	Cheese	Cheese
12	Red meat and products	Red meat, hamburger, and sausages
13	Fast fried foods	French fries and pizza
14	Pastries and sweets	Confections, ice cream, biscuit, cake, chocolate, candy, gaz (an Iranian confectionery made of sugar, nuts, and tamarisk), and gooshfil (an Iranian confectionery made of white flour and sugar)

### **Ethical considerations**

The Ethics Committee (IR. LUMS. REC.1399.308) of Lorestan University of Medical Sciences approved this case control research. Informed consent was obtained from every participant. Two groups then were matched for age and gender. The required questionnaires were filled out by the interviewers who were proficient in questionnaires and measurement modules.

### **Data analysis**

The Kolmogorov–Smirnov test was employed to evaluate the normality of the data distribution. Differences in continuous variables among the different quantiles of the MIND diet were analyzed using one-way analysis of variance (ANOVA). The examination of qualitative variables to assess variations among MIND diet quantiles was performed through cross-tabulation. The significance level for all tests was set at a probability of 0.05 or less. All statistical analyses

were conducted using IBM SPSS version 22.0 (SPSS, Chicago, IL, USA).

### **Results**

A total of 876 participants participated in the present study (315 in the case group vs 561 in the control group). The mean±SD of age was 29.72±10.19 and 32.14±10.91 years in the case group and the control group, respectively. The mean body weight for the case and control groups was 72.66±12.06 and 73.74±12.24 kg, respectively. In addition, the mean BMI for the case group was 25.84±3.87, while for the control group, it was 25.67±3.87 kg/m<sup>2</sup>.

**Table 2** illustrates the relationship between the participants' qualitative characteristics and the quantiles of the MIND diet score. A significant correlation was found between the quantiles of the MIND diet score and sex, educational status, marital status, job status, and smoking ( $P<0.001$ ).



**Table 2.** Number of participants across quantiles of MIND diet score.

Variables	Q1	Q2	Q3	Q4	Q5	P-value <sup>a</sup>
Gender						
Male	71	90	61	111	66	<0.001
Female	78	78	50	61	100	
Group						
Case	79	65	57	71	43	<0.001
Control	95	112	78	140	136	
Smoking						
Smoker	63	85	52	86	61	<0.001
Non-smoker	104	61	69	87	109	
Quit smoking	1	16	3	13	9	
Education status						
Illiterate	21	14	5	18	32	<0.001
Under high school diploma	22	11	17	12	12	
High school diploma	37	33	26	35	33	
Educated	77	107	73	136	96	
Job status						
Unemployed	47	54	32	67	33	<0.001
Housekeeper	53	59	62	89	90	
Employee	50	39	32	27	42	
Retired	0	0	0	1	0	
Farmer	7	10	0	7	0	
Marital status						
Single	85	87	54	111	122	<0.001
Married	85	82	71	82	47	

<sup>a</sup>: Chi-square test.

**Table 3** displays the participants' food intake across various quantiles of the MIND score. The ANOVA test indicated a significant difference in all food groups across these quantiles ( $P<0.01$ ). Mean $\pm$ SD of age, body weight, BMI, and IBS symptom severity across MIND score quintiles is presented in **Table 4**. Additionally, it was observed that the severity of IBS symptoms was significantly lower in quintiles 5 compared to the first quintile ( $P<0.001$ ). Also, a significant difference was found between the quantiles of the MIND diet and BMI and weight. However, no significant difference was observed between the lowest and the highest quintiles of the MIND score and age ( $P>0.05$ ). Before adjusting for confounders, a significant negative association was observed between the MIND diet and the odds of IBS ( $P<0.001$ ). In addition, after adjusting for confounders (age and sex, BMI, total energy intake, physical activity, educational status, marital status, smoking and drug use), a significant relationship was observed between adherence to

the MIND diet and the odds of IBS ( $P<0.001$ ) (**Table 5**).

### Discussion

Given the notable prevalence of IBS in Iran, recognizing and adjusting its contributing factors is highly important. The current case-control study aims to detect the relationship between MIND diet score and odds of IBS. The results showed that individuals in the top category of MIND diet score were 27% less likely to have IBS compared with those in the bottom category.

The results regarding the association MIND diet score and IBS are consistent with some previous studies. A study conducted in Southern Italy indicated a negative correlation between following the Mediterranean diet and the occurrence of gastrointestinal symptoms (Zito *et al.*, 2016). Moreover, a cross-sectional study revealed that following a lactovegetarian diet was linked to a lower prevalence ratio (PR) of IBS; conversely, following a fast food diet was connected to a

higher PR of IBS (Khayatzadeh *et al.*, 2016). A different cohort study indicated that a Western dietary pattern characterized by high intake of fatty and sugary foods and snacks was linked to increased risk of IBS (Buscail *et al.*, 2017). Similarly, Agakidis *et al.* studied 1,116 Greek

children and discovered that strong adherence to Mediterranean diet (MD) correlated with a lower prevalence of gut-brain interaction disorders, including functional constipation, IBS, and functional dyspepsia per the Rome III criteria (Agakidis *et al.*, 2019).

**Table 3.** Food groups across quantiles of MIND diet score.

Food groups	Q1	Q2	Q3	Q4	Q5	P-value <sup>a</sup>
Green leafy vegetables	13.28±10.03 <sup>b</sup>	21.48±17.83	23.80±22.26	29.21±17.90	32.96±21.30	<0.001
Other vegetables	127.57±123.17	160.94±143.40	222.00±178.34	279.52±210.60	277.92±160.54	<0.001
Berries	0.97±2.11	1.92±3.80	2.00±4.83	2.09±3.60	3.12±5.94	<0.001
Nuts	1.52±1.87	2.47±5.58	3.97±4.22	5.87±9.43	7.23±13.80	<0.001
Whole grains	16.61±17.63	16.33±18.43	14.96±12.89	18.90±19.35	38.44±30.21	<0.001
Fish	2.02±5.52	1.52±1.81	3.97±7.83	4.84±5.37	9.38±7.57	<0.001
Beans	11.14±12.70	23.17±22.96	16.53±12.01	25.66±27.10	22.01±11.22	<0.001
Poultry	20.29±21.89	27.34±24.77	27.13±26.52	37.68±31.09	50.58±51.71	<0.001
Olive oil	0.05±0.23	0.01±0.11	0.01±0.05	0.22±1.03	0.08±0.36	0.001
Butter and margarine	4.76±17.83	2.95±28.33	6.20±14.07	12.08±4.97	5.43±7.64	<0.001
Cheese	11.33±14.14	17.96±19.42	11.85±22.79	17.22±24.83	14.11±19.71	<0.001
Red meat and products	24.03±23.87	18.28±23.42	15.95±19.17	27.98±50.38	21.98±41.78	0.01
Fast fried foods	11.79±13.02	13.11±15.73	15.13±15.48	18.18±13.13	14.73±11.56	<0.001
Pastries and sweets	32.67±39.38	21.74±27.64	21.37±29.33	31.18±48.81	18.34±23.56	<0.001

<sup>a</sup>:ANOVA test; <sup>b</sup>: Mean±SD.

**Table 4.** Components of demographics and severity of irritable bowel syndrome symptoms across quantiles of MIND diet score.

Variables	MIND score quantiles					P-value <sup>a</sup>
	Q1	Q2	Q3	Q4	Q5	
Age (year)						
Case (n =315)	32.87±13.43 <sup>b</sup>	26.46±5.16	26.85±6.15	30.74±11.50	30.53±9.03	<0.001
Control (n =510)	30.97±8.99	32.74±10.84	35.25±12.02	31.21±11.27	33.39±11.54	0.07
Body weight (kg)						
Case (n =312)	71.85±11.08	69.66±7.52	69.85±12.85	78.74±14.29	72.70±11.65	<0.001
Control (n =547)	72.26±10.78	70.89±13.21	74.00±11.69	75.64±13.01	74.21±11.76	0.03
Body mass index (kg/m <sup>2</sup> )						
Case (n =312)	26.09±3.35	24.53±2.66	25.36±4.94	27.12±3.89	26.00±4.14	<0.001
Control (n =547)	25.59±3.44	25.04±4.30	25.97±3.32	25.89±4.08	25.70±4.08	0.85
Severity of symptoms in IBS patients						
Case (n = 315)	0.59±0.49	0.66±0.47	0.70±0.45	0.76±0.42	0.58±0.49	0.01

<sup>a</sup>:ANOVA test; <sup>b</sup>: Mean±SD.

In contrast to the results of the present study, in 2021, Altomare *et al.* carried out a pilot study in Italy, examining dietary habits and IBS symptoms

in 28 IBS participants and 21 healthy controls. No association was found between MD adherence and IBS symptoms such as abdominal pain and

flatulence (Altomare *et al.*, 2021). Chen *et al.* in a cross-sectional study revealed that alternate Mediterranean diet and Mediterranean diet adherence screener scores were similar between IBS and health control subjects who did not correlate with IBS severity scoring system, abdominal pain, or bloating (Chen *et al.*, 2024). Also, in another cross-sectional study conducted in Iranian adults, no significant relationship was found between compliance with the MIND diet and the likelihood of IBS (Nouri-Majd *et al.*, 2022). Additionally, when they divided analyses by gender and BMI status, no notable association was detected (Nouri-Majd *et al.*, 2022).

**Table 5.** Odds ratio (95 % CI) of irritable bowel syndrome symptoms based on MIND diet.

Models	OR	CI	P-value
Crude	0.81	0.71 to 0.92	<0.001
Model 1	0.78	0.68 to 0.89	<0.001
Model 2	0.75	0.65 to 0.87	<0.001
Model 3	0.73	0.63 to 0.85	<0.001

Analysis performed by binary logistic; **IBS**: Irritable bowel syndrome; **OR**: Odds ratio; **CI**: Confidence interval; **Model 1**: adjusted for age and sex; **Model 2**: BMI, total energy intake and physical activity; **Model 3**: additionally adjusted for educational status, marital status, smoking and drug use.

The discrepancies of the results could be attributed to the elevated levels of fermentable oligosaccharides, disaccharides, monosaccharides, and polyols (FODMAPs) present in this eating pattern. Earlier research indicated that a low-FODMAP diet was linked to reduced IBS symptoms (Nawawi *et al.*, 2020). Certain elements of the MIND diet, like vegetables and beans, contain a high level of FODMAPs. Given the cross-sectional design of this research, reverse causality may arise, meaning that IBS patients might exhibit poor adherence to the MIND diet due to its elevated FODMAP levels. Furthermore, the MIND diet particularly emphasizes the intake of berries. In those researches, the berries category consists solely of strawberries and blueberries. Berries are not present throughout the year in Iran; they are only accessible for 3–4 months annually. Consequently, the intake of berries, a significant

component of the MIND diet, was relatively low in the study population. This could, at least partially, influence the results. Due to the insufficient research on the link between following the MIND diet and IBS, additional studies are needed to clarify this matter.

The MIND diet merges the Mediterranean and DASH diets, focusing on the intake of vegetables and berries while limiting the consumption of animal products and foods high in saturated fats (Morris *et al.*, 2015). The authors posited that there would be a notable negative association between the MIND diet and the likelihood of IBS. This hypothesis was grounded in the observation that the MIND diet influences mental well-being (Salari-Moghaddam *et al.*, 2019, Torabynasab *et al.*, 2023), considering the significant impact of mental health on IBS and its symptoms (Koloski *et al.*, 2020). In this study, the researcher's hypothesis regarding the association between adherence to the MIND diet and IBS was accepted.

A thorough comprehension of the ways in which the MIND diet might affect brain health has yet to be established. Given the significance of oxidative stress in psychological conditions, it seems that the MIND diet could serve as a protector of brain health due to its antioxidant and anti-inflammatory effects (Salim, 2014). The MIND diet is an excellent source of vitamins, minerals, and flavonoids that serve antioxidant and anti-inflammatory purposes, which contribute to brain protection. Additionally, following MIND dietary guidelines involves limiting pro-inflammatory food categories such as red meat and related products, sweets and desserts, butter, and fast food. Changes in gut microbiota represent another way the MIND diet influences brain health. Inflammatory conditions can be initiated by alterations in GI microbiota composition after ingesting pro-inflammatory foods like fats, sugars, and processed carbs instead of fiber, vegetables, and whole grains (Solas *et al.*, 2017, Telle-Hansen *et al.*, 2018). Although there is no exact predefined mechanism, alterations in plasma concentrations of lipopolysaccharides (LPS) and the signaling pathways of inflammation, interferon type I, and

Nuclear factor kappa B (NF- $\kappa$ B) are thought to be implicated (Ma *et al.*, 2019).

There are several noteworthy strengths in this study that deserved to be highlighted. First of all, to the authors' knowledge, this is the first case-control study which examines the relationship between MIND diet score and IBS odds. Second, the classification of the participants was based on gastroenterology subspecialist diagnosis applying the available sampling method. Furthermore, a validated food frequency questionnaire was used to assess dietary intake, which provided more accurate results compared to other methods. Finally, suitable sample size, careful assessment of confounding factors and their control in the analyses could be considered as the other strengths of the present study

Several key limitations were also taken into account. Due to the nature of this observational study design, the authors are unable to establish causal relationships and may have missed residual confounders that they did not consider in this analysis. Various confounders were examined, including demographics, anthropometrics, lifestyle, and clinical factors, and were accounted for their effects in the analysis. In this research, a validated FFQ was utilized to evaluate the dietary intakes of the study participants. Nonetheless, misclassification of individuals regarding exposure is unavoidable. Moreover, wine was excluded from the scoring process because of insufficient data in the FFQs.

### Conclusion

In conclusion, the findings from this case-control study offered evidence suggesting a negative association between adherence to the MIND diet and the likelihood of developing IBS. Ultimately, because of the potential protective influence of diet, it is essential to elucidate the connection between diet and psychological disorders through extensive prospective cohort studies in the future.

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### Authors' contributions

Abbasnezhad A contributed to conception/design of the research; Mohammadi S and Samadi M assisted with acquisition, analysis, or interpretation of the data; Fazeli Moghadam E and Yarizadeh H drafted the manuscript; HS and Fazeli Moghadam E critically revised the manuscript, and Shahinfar H agrees to be fully accountable for ensuring the integrity and accuracy of the work. All authors read and approved the final manuscript.

### Conflict of interest

The authors declared no competing interests.

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