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The Association between Adherence to the MIND Diet and Depression and Anxiety in Irritable Bowel Syndrome Patients

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ABSTRACT

Background: Irritable Bowel Syndrome (IBS) is one of the most common functional gastrointestinal disorders. Accordingly, this study aims to investigate the association between adherence to the Mediterranean-DASH Intervention for Neurodegenerative Delay (MIND) diet and the odds of anxiety and depression among patients with IBS. **Methods:** This multicenter cross-sectional study was conducted from 2021 to 2023 in three university-affiliated centers in Iran. A total of 262 IBS patients aged 18–60 (168 males, 94 females; mean age 29.72 ± 10.19 years) were recruited based on the Rome III criteria. Dietary intake was assessed using a validated 168-item food frequency questionnaire, and MIND diet scores were calculated. Anxiety was measured using the Hospital Anxiety and Depression Scale (HADS), and depression was assessed using the Patient Health Questionnaire-9 (PHQ-9). Logistic regression analyses were performed to estimate the odds ratios (ORs) for anxiety and depression across MIND diet score tertiles, adjusting for potential confounders. **Results:** Higher adherence to the MIND diet was significantly associated with lower odds of both anxiety (OR: 0.69, 95% CI: 0.53–0.89, *P*=0.005) and depression (OR: 0.73, 95% CI: 0.59–0.91, *P*=0.006) in IBS patients. Additionally, an inverse relationship was observed between MIND diet adherence and the severity of IBS symptoms (OR: 0.70, 95% CI: 0.52–0.94, *P*=0.02). **Conclusion:** Greater adherence to the MIND diet was associated with reduced odds of anxiety and depression, as well as lower severity of IBS symptoms. Further prospective and interventional studies are warranted to confirm these findings.

Introduction

Irritable Bowel Syndrome (IBS) is among the most prevalent functional bowel disorders; it is a type of functional gastrointestinal disorder (FGID) that involves persistent abdominal pain or discomfort along with changes in bowel habits (Shaikh *et al.*, 2023). The meta-analysis results indicated that the global prevalence of IBS was 9.2% (Oka *et al.*, 2020). In Iran, reported prevalence rates of IBS

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ranged from 1.1% to 25%, with a higher occurrence observed among women (Jahangiri *et al.*, 2012).

IBS indeed has a significant impact on healthcare systems (Canavan *et al.*, 2014). Research shows that patients with IBS often experience higher levels of depression and anxiety compared to those without IBS (Zamani *et al.*, 2019). This psychological distress can exacerbate gastrointestinal symptoms, creating a challenging cycle for patients (Midenfjord *et al.*, 2019). In humans, several types of brain networks have been identified. Alterations in neural networks related to IBS have provided plausible neurobiological substrates for various information-processing abnormalities observed in patients with IBS (Mayer *et al.*, 2023). Results of a meta-analysis have shown that individuals with IBS experience anxiety compared to the general population (Lee *et al.*, 2017).

Several factors contribute to the pathogenesis of IBS, including dysregulated brain-gut communication (brain-gut axis), alterations in the gut microbiome, previous infections, psychological stress, dietary influences, and both pre- and postnatal factors (Shaikh *et al.*, 2023).

Diet can influence both irritable bowel syndrome symptoms and mental health disorders (Chen *et al.*, 2024, Grajek *et al.*, 2022). A 2024 study found that consuming a low-fermentable oligosaccharides, disaccharides, mono saccharides, and polyols (FODMAP) diet combined with prebiotics reduced depression, anxiety, IBS, quality of life scale and the severity of symptoms in patients with IBS (Ustaoğlu *et al.*, 2024). Previous studies have demonstrated that DASH and Mediterranean diets positively impact quality of life, as well as anxiety and depression (Shiraseb *et al.*, 2023, Tan *et al.*, 2024). The Mediterranean-DASH Intervention for Neurodegenerative Delay diet (MIND) diet, a combination of the Mediterranean and DASH diets, effectively bridges the gaps by integrating the strengths of both. It focuses on specific dietary components that enhance brain health while avoiding harmful food choices. The MIND diet includes ten components that promote brain health: green leafy vegetables, other vegetables, nuts, berries, beans, whole grains, fish, poultry, olive oil, and wine. It avoids five unhealthy components: red meats, butter and stick margarine, cheese, pastries and sweets, and fried or fast foods (Kheirouri and Alizadeh, 2022). Studies on the association between the MIND diet and mental disorders have yielded inconsistent results, with some finding an inverse relationship and others finding no significant association (Seifollahi *et al.*, 2024, Torabynasab *et al.*, 2023).

In this study, the authors aim to investigate the relationship between the Mind diet and depression, as well as anxiety in Iranian patients with IBS.

Materials and Methods

Study design and participant enrollment

This multicenter cross-sectional study was conducted from 2021 to 2023 at Lorestan University of Medical Sciences (Khorramabad), Urmia University of Medical Sciences and Kermanshah University of Medical Sciences. In this study, IBS patients aged 18 to 60 years old who were referred to the specialized clinics of the mentioned universities were selected from each center based on the Rome III diagnostic criteria with the approval of the gastroenterology subspecialist using the convenience sampling method. These criteria define IBS as recurrent abdominal pain or discomfort occurring at least three days per month during the past three months, accompanied by at least two of the following: (1) improvement of symptoms with defecation, (2) onset associated with a change in stool frequency, and (3) onset associated with a change in stool form. Individuals with underlying conditions such as diabetes, liver or kidney dysfunction, cardiovascular disease, cancer, coeliac disease, inflammatory bowel disease, or other digestive disorders, as well as those with a history of abdominal surgery, pregnancy, breastfeeding, special diets, smoking, or alcohol consumption, were excluded from the study.

Measurements

The dietary intake was assessed using the

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previously validated and reliable 168-item Food Frequency Questionnaire (FFQ) (Bawadi *et al.*, 2021). In this questionnaire, there is a standard size for each food item, which is designed according to the Willette 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, and finally, the exact amounts of energy, micronutrients, and macronutrients consumed by each participant were calculated using the Nutritionist IV (N4) software.

MIND diet assessment: The assessment of dietary intake was conducted through face-to-face interviews using a validated 168-item semi-quantitative FFQ tailored for Iran. For this study, specific nutritional components from the FFQ, detailed in **Table 1**, were used to compute MIND diet scores. Out of the original 15 dietary components in the MIND diet, 10 were classified as beneficial to brain health-these include green leafy vegetables, other vegetables, nuts, berries, beans, whole grains, fish, poultry, olive oil, and wine—while 5 were deemed harmful: red meats, butter and stick margarine, cheese, pastries, and sweets, and fried/fast food. In this study, the authors utilized a modified MIND diet scoring system adjusted for Iranian dietary customs by excluding wine, consumption of which is not legally permitted. Scoring for the MIND diet was applied to the remaining 14 food groups. Participants were divided into tertile categories based on their intake levels. Participants in the lowest tertile of brain-healthy foods received a score of 0, those in the middle tertile received 0.5, and individuals in the highest tertile were given a score of 1. Conversely, the unhealthy food groups were evaluated in reverse. The total MIND diet score ranged from 0 to 14, summing the scores from all dietary components.

Table 1. Components of the MIND diet score.

Brain-Healthy foods score		
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, chickpeas, mung beans, and cotyledons
8	Poultry	Chicken
9	Olive oil	Olive oil
Brain-unhealthy foods score		
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)

Severity of IBS symptoms: The Extra-Intestinal Symptoms Severity Scale (EISSS) was used to assess the severity of extra-intestinal IBS symptoms. This instrument consists of 15 seven-

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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, heartburn, urgency to defecate, feeling of incomplete bowel movement, urgency to urinate, thigh pain, muscle or joint pain, and 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).

Severity of depression symptoms: The Patient Health Questionnaire (PHQ-9) was used to assess depression severity. This questionnaire consists of 9 items and ranges from 0 to 27 regarding the intensity of depression symptoms. A score of less than 5 indicates mental health and the absence of depression, while a score between 5 and 9 indicates mild depression. Scores between 10 and 14 or above 15 represent moderate to severe depressive states, respectively. Individuals with a depression score of 10 or higher were considered depressed patients (Kroenke *et al.*, 2001).

Anxiety status: The Hospital Anxiety and Depression Scale (HADS) questionnaire was used to assess participants' anxiety status. This questionnaire consists of 14 self-reported questions, each scored on a 4-point Likert scale ranging from 0 to 3. A participant's total score would range from 0 to 21. Lower scores indicate less anxiety, and individuals with an anxiety score of 11 or higher were considered depressed (de Lemos Zingano *et al.*, 2019).

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 BMI was calculated by dividing the body weight (kg) by the height (m^2) (Ramstrand *et al.*, 2011).

Physical activity level: The physical activity of the participants was assessed using the International Physical Activity Questionnaire (IPAQ). 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 (Mohammadi *et al.*, 2022).

Ethical considerations

The ethical committee of Lorestan University of Medical Sciences approved the study (code number:IR.IUMS.REC.1399.308). The written informed consent was signed by all the participants before the beginning of the study. This study was performed in line with the ethical principles established by the World Medical Association in the Declaration of Helsinki.

Data analysis

The Kolmogorov–Smirnov test was used to assess the normality of the data distribution. One-way analysis of variance (ANOVA) was employed to analyze differences in continuous variables across different quantiles of the MIND diet. For qualitative variables, variations among MIND diet quantiles were examined using cross-tabulation. Logistic regression was performed to examine prevalence ratio of psychological disorders in IBS patients in a crude model and three justified models; they included the crude model which was justified for no variable, model-1 justified for age and gender, model-2 additionally justified for BMI and total energy intake, and model-3 which was additionally justified for educational status, and marital status. A significance level of 0.05 or lower was established for all tests. All statistical analyses were performed using IBM SPSS version 22.0 (SPSS, Chicago, IL, USA).

Results

Study population

A total of 262 IBS patients were involved in this study (168 males, 94 females), and the average age was 29.72±10.19 years. The mean body weight and BMI were 72.66±12.06 kg and 25.84±3.87 kg/m², respectively. The differences in age, BMI and body

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weight across the various MIND score quantiles are presented in **Table 2**.

Food intake

Table 3 illustrates the participants' food consumption across different quantiles of the MIND score. The results from the ANOVA test revealed significant differences in all food groups among these quantiles (P<0.01).

Qualitative characteristics

Table 4 shows how the participants' qualitative characteristics relate to the quantiles of the MIND diet score. A significant correlation was observed between the MIND diet score quantiles and factors such as sex, educational status, marital status, job status, smoking habits, depression status, anxiety status and severity of IBS symptoms (P<0.001).

MIND diet, depression and anxiety

According to the findings, there was a significant correlation between anxiety status and MIND score (Spearman correlation r: - 0.21, P=0.003). Prevalence ratio of anxiety and depression among IBS patients based on MIND score quintiles is presented in **Table 5**. As shown in this table, A significant negative relationship was observed between the MIND diet and the prevalence ratio of anxiety (95 % CI: 0.69, 0.53 to 0.89, P=0.005) and depression (95 % CI: 0.73, 0.59 to 0.91, P=0.006) in individuals with IBS after adjusting for confounding variables such as age, sex, BMI, total energy intake, educational status, and marital status.

MIND diet and severity of IBS symptoms

The binary logistic regression model showed a significant inverse relationship between the MIND diet and the severity of IBS symptoms (OR 0.70, 95% CI 0.52 to 0.94, P=0.02) in the IBS group, even after controlling for confounding variables (age, gender, total energy intake, physical activity, educational status, and marital status). However, this association was not observed in the healthy group (**Table 6**).

Discussion

To the best of the authors' knowledge, this is the first study to investigate the relationship between the MIND diet and depression and anxiety in individuals with irritable bowel syndrome. Results of this study showed that there was a negative relationship between the MIND diet and the prevalence ratio of depression and anxiety in people with IBS.

The well-documented co-occurrence of IBS with anxiety and depression is widely recognized. Both conditions share various biological and psychosocial mechanisms, many of which lead to a disrupted gut-brain axis (Staudacher *et al.*, 2021). Meta-analyses have demonstrated that individuals with IBS exhibit higher levels of anxiety and depression compared to healthy controls (Zamani *et al.*, 2019).

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

Variables	Q1	Q2	Q3	Q4	Q5	P-value[a]
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	
Non-smoker	104	61	69	87	109	<0.001
Quit smoking	1	16	3	13	9	
Education						
Illiterate	21	14	5	18	32	
Under high school diploma	22	11	17	12	12	<0.001
High school diploma	37	33	26	35	33	
Educated	77	107	73	136	96	
Job status						
Unemployed	47	54	32	67	33	
Housekeeper	53	59	62	89	90	<0.001
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	

[a]: *Obtained from Chi-square test*

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

Food groups	Q1	Q 2	Q 3	Q 4	Q 5	P-value[a]
Green leafy vegetables	42.33±20.69	28.16±19.15	22.26±13.35	18.51±14.04	10.18±8.78	<0.001
Other vegetables	341.13±199.84	263.77±201.39	197.01±142.22	165.59±106.55	108.88±108.34	<0.001
Berries	6.83±0.49	4.83±0.36	1.09±0.09	1.24±0.09	0.79±0.05	<0.001
Nuts	11.53±15.86	3.17±3.21	2.67±2.46	2.55±2.22	0.98±1.59	<0.001
Whole grains	34.45±29.75	21.15±19.88	24.52±21.42	15.14±15.64	11.55±14.45	<0.001
Fish	8.09±7.86	6.02±8.12	2.72±4.13	3.96±5.70	0.95±1.19	<0.001
Beans	31.22±27.44	18.28±13.71	22.87±20.61	17.23±16.25	11.32±9.56	<0.001
Poultry	52.43±54.26	38.92±27.67	26.15±18.46	28.80±25.17	17.95±20.51	<0.001
Olive oil	0.22±1.02	0.08±0.47	0.06±0.31	0.04±0.23	0.00±0.03	0.002
Butter and margarine	18.93±33.52	5.70±8.19	4.61±7.53	1.70±2.79	0.71±1.44	<0.001
Cheese	25.44±29.88	19.90±21.63	13.37±17.14	9.67±11.13	5.00±7.73	<0.001
Red meat and products	44.21±61.26	27.13±27.09	19.27±19.73	12.68±12.52	6.42±9.76	<0.001
Fast fried foods	23.50±15.99	19.02±13.16	14.83±13.68	9.64±9.57	6.54±9.02	<0.001
Pastries and sweets	44.45±49.83	26.83±30.13	33.57±43.17	14.02±13.73	9.40±18.48	<0.001

[a]*: Obtained from ANOVA test.*

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

Variables	Q1	Q 2	Q 3	Q 4	Q 5	P-value[a]
Age (year)	30.35±9.99	33.72±12.63	31.61±11.05	31.70±10.49	30.08±9.52	0.01
Body weight (kg)	73.88±12.57	73.50±11.78	72.47±11.72	74.27±12.81	72.05±12.15	0.37
Boy mass index(kg/m^2)	26.25±3.47	25.25±3.90	25.56±4.37	25.61±4.14	26.00±3.70	0.13
Severity of symptoms	32.92±8.45	27.62±9.96	29.38±7.35	28.59±8.78	31.22±9.06	<0.001

[a]*: Obtained from ANOVA test.*

Table 5. Odds ratio (95 % CI) for risk of depression and anxiety based on MIND diet in individuals with IBS.

Variables	IBS			Healthy		
	OR	CI	P-value[a]	OR	CI	P-value[a]
Depression						
Crude	0.74	0.60 to 0.91	0.005	0.99	0.85 to 1.16	0.98
Model 1	0.75	0.60 to 0.92	0.008	0.97	0.83 to 0.14	0.77
Model 2	0.72	0.58 to 0.90	0.004	0.98	0.83 to 1.15	0.83
Model 3	0.73	0.59 to 0.91	0.006	0.95	0.80 to 1.12	0.55
Anxiety						
Crude	0.64	0.51 to 0.82	<0.001	0.91	0.78 to 0.106	0.26
Model 1	0.63	0.50 to 0.81	<0.001	0.91	0.78 to 0.106	0.23
Model 2	0.65	0.51 to 0.83	0.001	0.92	0.79 to 1.07	0.32
Model 3	0.69	0.53 to 0.89	0.005	0.92	0.79 to 1.08	0.35

[a]: Obtained from *binary logistic regression; **IBS**: Irritable bowel syndrome, **OR**: Odds ratio; **CI**: Confidence interval; **Model 1**: adjusted for age and sex; **Model 2**:BMI and total energy intake; **Model 3**: additionally adjusted for educational status, and marital status*.

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Table 6. Odds ratio (95 % CI) for risk of severity of symptoms based on MIND diet.

	IBS			Healthy		
Depression	**OR**	**CI**	**P-value[a]**	**OR**	**CI**	**P-value[a]**
Crude	0.76	0.58 to 0.99	0.04	0.97	0.83 to 1.13	0.70
Model 1	0.80	0.61 to 0.1.05	0.11	0.39	0.79 to 1.09	0.93
Model 2	0.68	0.50 to 0.92	0.01	0.94	0.80 to 1.11	0.48
Model 3	0.07	0.52 to 0.94	0.02	0.97	0.82 to 1.15	0.80

[a]: Obtained from *binary logistic regression; **IBS**: Irritable bowel syndrome, **OR**: Odds ratio; **CI**: Confidence interval; **Model 1**: adjusted for age and sex; **Model 2**:BMI and total energy intake; **Model 3**: additionally adjusted for educational status, and marital status*.

The gut-brain axis involves two-way communication between the central and enteric nervous systems, connecting the brain's emotional and cognitive centers with intestinal functions (Carabotti *et al.*, 2015, Stasi *et al.*, 2012). The hypothalamic-pituitary-adrenal (HPA) axis is key in regulating behavioral, neuroendocrine, and autonomic stress responses. Under stress, the autonomic nervous system triggers the release of corticotrophin-releasing factor (CRF) through the HPA axis, potentially disrupting gastrointestinal function (Dinan *et al.*, 2006). Stress can elevate systemic proinflammatory cytokines, which can activate the HPA axis at the pituitary and send signals to the central nervous system through the vagus nerve (Kennedy *et al.*, 2012). This can affect the GI tract, possibly due to the activation of eosinophils and mast cells in the intestinal lining, as observed in patients with IBS and FD (Walker *et al.*, 2014) .

Diet can significantly influence the HPA axis, which plays a crucial role in stress response and overall health (Staudacher *et al.*, 2024). Some studies have demonstrated that antioxidants can influence the HPA axis (Ge *et al.*, 2016, Prevatto *et al.*, 2017). For example, the results of experimental study indicate that resveratrol produces anxiety-reducing and antidepressant-like effects in rats with subclinical hypothyroidism by decreasing the overactivity of the HPA axis and modulating both the HPT axis and the Wnt/β-catenin pathway (Ge *et al.*, 2016).

The MIND diet, similar to its component diets, highlights the importance of eating plant-based foods such as leafy green vegetables, nuts, berries, fish, and olive oil. It restricts the consumption of foods high in saturated fat and sugar, including red or processed meats, butter, margarine, full-fat cheese, pastries, sweets, and fried foods. (Barnes *et al.*, 2023) The MIND diet is rich in omega-3 fatty acids, antioxidants, and various other nutrients that support brain health and cognitive function (Kamrani *et al.*, 2024). A cross-sectional study investigated the relationship between HPA axis activity and fatty acid metabolism in adults diagnosed with recurrent depressive disorder (Thesing *et al.*, 2018). The association between HPA-axis activity and fatty acid metabolism in adults with recurrent depressive disorder was studied. It was found that adults with low levels of omega-3 fatty acids exhibited a dysregulated HPA axis, indicating that treatment with these fatty acids could enhance both physical and mental health (Thesing *et al.*, 2018). Results of clinical trials have shown that a 12-week supplementation with omega-3 fatty acids in adolescents with depression reduced morning salivary cortisol levels. However, this reduction was not seen in patients with mixed anxiety and depressive disorder but was notably significant in those with depressive disorder (Oravcova *et al.*, 2022). Results of cross sectional study demonstrated that individuals with IBS, a high n-6/n-3 PUFA ratio was linked to increased depressive symptoms (Sanders *et al.*, 2022).

IBS patients often experienced anxiety, which was linked to the severity of their symptoms (Cho *et al.*, 2011). The study results indicate that adhering to the MIND diet can reduce the prevalence ratio of anxiety in patients with IBS.

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The previous studies were inconsistent with the results of the current study. The findings of a cross-sectional study showed no significant association between adherence to the MIND diet and the odds of anxiety (Salari-Moghaddam *et al.*, 2019). Another study also reported no significant association between the MIND diet score and anxiety (Ardekani *et al.*, 2023). However, the results of one study contradicted previous findings, showing a negative association between adherence to the MIND diet and both the odds and severity of anxiety (Torabynasab *et al.*, 2023). Changes in gut microbiota are another way the MIND diet affects brain health. Inflammatory conditions may arise from changes in the composition of gut microbiota caused by consuming pro-inflammatory foods such as fats, sweets, and processed carbohydrates, rather than fiber, vegetables, and whole grains (Torabynasab *et al.*, 2023).

To the best of the researchers' knowledge, this study is the first to examine the relationship between the MIND diet score and mental health in individuals with IBS. Additionally, dietary intake was evaluated using a validated FFQ, and potential confounders were accounted for using appropriate statistical methods. This study had some limitations. The cross-sectional design made it difficult to establish a causal link between the MIND diet and mental health. Additionally, the FFQ's reliance on participants' memory may have introduced measurement errors. Furthermore, wine was not included in the scoring process due to insufficient information in the FFQs.

Conclusion

This study showed that following the MIND diet can lower prevalence ratio of anxiety and depression in IBS patients. This diet is rich in components that promote brain health, including green leafy vegetables, other vegetables, nuts, berries, beans, whole grains, fish, poultry, olive oil, and wine. Further clinical trials are required to validate these findings.

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Authors' contributions

Abbasnezhad A designed the study; Fazeli Moghadam E, Abbasnezhad A and Samadi M conducted the study; Mohammadi M, Darabi Z, Fazeli Moghadam E, and Yarizadeh H wrote the manuscript and were involved in the analysis; Fazeli Moghadam E supervised the study. The final version of the manuscript was approved by all the authors.

Confilict of interests

The authors declared no competing interests.

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