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Adherence to a low-fat, high-protein diet and gastroesophageal reflux disorder among Iranian adults

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A B S T R A C T

Objective: This study was performed to determine the association between consumption of low-fat, high-protein diet and GERD in a large group of the Iranian population.
Methods: This cross-sectional study was done on 3362 participants. We used a validated self-administered, dish-based semi-quantitative food frequency questionnaire (FFQ) with multiple choice frequency response categories for assessing usual dietary intakes. Dietary fat and protein intakes were obtained from the FFQ. We defined GERD as the presence of heartburn sometimes, often, or always during the three months prior to the study.
Results: Dietary fat intake was not significantly associated with GERD, even after further controlling for confounding factors including BMI (Odds ratio [OR] for comparing highest vs. lowest quartiles of fat intake: 1.11; 95% CI: 0.96-1.78). Similar findings were made for protein intakes, such that those with the highest protein intakes did not have a significantly reduced odds for GERD, either before (OR: 0.83; 95% CI: 0.67-1.04) or after adjustment for potential confounders (OR: 0.97; 95% CI: 0.56-1.67) including BMI (OR: 0.84; 95% CI: 0.48-1.47). Adherence to a low-fat, high protein diet was not significantly associated with the odds of GERD. Even after adjustment for potential confounders, including diet-related variables, we found no significant association between adherence to a low-fat, high-protein diet and odds of GERD. Additional controlling for BMI did not significantly alter this result.
Conclusion: In this large-scale cross-sectional study among Iranian adults, we failed to find any significant association between adherence to a low-fat high-protein diet and odds of GERD. It seems that more studies with different designs are needed to achieve a definitive conclusion.

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Introduction

Gastroesophageal reflux disorder (GERD) is a chronic condition due to the retrograde flow of gastroduodenal contents [1]. It might be associated with esophagitis/esophageal ulcer and

upper GI bleeding [1]. It is also associated with an increased risk of extraesophageal complications, including respiratory disorders, chest pain, and angina [2]. The prevalence of GERD varies from 10% to 38% in Western populations [1]. In Iran, the prevalence has been estimated to be up to 33% among adults [2].

Several dietary and nondietary factors have been linked with the symptoms of GERD. Among nutritional factors, consumption of canned foods and drinking alcohol and caffeine were associated with the severity of GERD [3]. Although fat and carbohydrate intakes have separately been examined in relation to GERD, data on the association of the combination of macronutrients with this condition are scarce. Most studies have reported that consumption of high-fat diets was associated with a greater risk of GERD, whereas high-fiber diets were inversely associated with GERD [4-9]. However, there are also studies that failed to find any significant association between dietary fat intake and GERD [10-12]. Regarding dietary protein intake, no large-scale study is available indicating its effects on GERD. Wu et al. showed an inverse association between protein intake and reflux disorder, while others were not able to show such an association [13].

Due to the improved economic situation, protein intake is increasing in developing countries. On the other hand, increased awareness of diet-health relationships has resulted in reduced dietary fat intake. Therefore, investigating the relationship between low-fat, high-protein diets and chronic conditions including GERD is interesting. In addition, it should be noted that most studies that investigated the relationship between macronutrient intake and reflux disorder were limited to Western societies, and data are scarce for Asian countries. Furthermore, earlier studies mostly did not take into account the dietary habits of the study participants when assessing diet-GERD relationships. This study was, therefore, performed to determine the association between consumption of a low-fat, high-protein diet and GERD in a large group of Iranian population while controlling for dietary habits.

Subjects and methods

Study participants: This cross-sectional study was done in the framework of the study on the Epidemiology of Psychiatric-Alimentary Health and Nutrition (SEPAHAN), a project carried out in Isfahan province, Iran, examining adults working in 50 different rural and urban health centers affiliated with the Isfahan University of Medical Sciences [14]. The study was conducted in two main phases. In the first phase, a self-administered questionnaire about socio-demographic factors, lifestyle factors, and dietary habits and intakes were distributed among 10087 people, 8691 of whom completed the questionnaires. In the second phase, functional gastrointestinal disorders were assessed using the ROME III diagnostic criteria. After merging data from the first and second phases, complete information on 3362 participants was available for analysis. The study was ethically approved jointly by the Medical Research Committee of the Isfahan University of Medical Sciences, Isfahan, Iran, and Tehran University of Medical Sciences, Tehran, Iran.

Assessment of dietary intake

We used a validated self-administered, dish-based, machine-readable, semiquantitative food frequency questionnaire (FFQ) to assess usual dietary intakes. The FFQ included 106 food items along with a given portion size [15]. Foods and dishes in the FFQ were classified into five main groups to facilitate responding: (1) mixed dishes, (2) grains, (3) dairy products, (4) fruits and vegetables, and (5) miscellaneous food items and beverages. The portion sizes used in the FFQ were obtained from our earlier studies that used dietary recalls and food records. The frequency for each food item could be selected from among 6 to 9 choices ranging from "never" to "≥ 12 times per day". The portion sizes for each food item were converted to grams using household measures. The reliability of the FFQ was assessed by comparing dietary intake estimates obtained the FFQ on 2 different occasions. The validity of the FFQ was assessed using three 24-h dietary records. Overall, these data indicated that the FFQ provided valid and reliable measures of the average long-term dietary intakes.

Classification of dietary patterns

Fat and protein intake scores were calculated for each participant. Then, based on the median score for each macronutrient, participants were classified as following a low-fat, low-protein (LFLP), low-fat, high-protein (LFHP), high-fat, low protein (HFLP), or high-fat, high-protein diet (HFHP). In order to estimate the relationship between the LFHP dietary pattern and risk of reflux, people with an HFLP diet were considered as reference, and the risk of GERD in the other 3 groups was calculated relative to the reference

Table 1: General characteristics of study participants across quartiles of protein and fat intake

	Quartiles of fat intake				P*	Quartiles of protein intake				P*
	Q1	Q2	Q3	Q4		Q1	Q2	Q3	Q4	
Age, means ± SD, y	36.5 ± 7.6	36.1 ± 8.1	36.0 ± 7.4	36.4 ± 8.2	0.55	36.5 ± 7.5	35.8 ± 7.7	35.7 ± 7.7	37.0 ± 8.3	0.005
Weight, means ± SD, kg	68.6 ± 13.1	67.9 ± 12.9	69.0 ± 13.3	69.0 ± 13.3	0.26	68.5 ± 13.6	67.6 ± 12.5	68.7 ± 13.3	69.6 ± 13.1	0.02
BMI, means ± SD, kg/m^2	25.2 ± 2	24.7 ± 3.7	24.9 ± 3.7	24.6 ± 3.8	0.01	25.1 ± 3.9	24.8 ± 3.8	24.8 ± 3.8	24.7 ± 3.6	0.12
Female, %	65	61	56	51	< 0.001	64	64	57	48	< 0.001
Married, %	84	80	83	80	0.22	84	81	82	80	0.16
Family size ≥4, %	11	13	14	13	0.53	12	12	12	15	0.14
Current smoker, %	14	12	14	15	0.001	14	13	14	14	0.01
University graduate, %	58	63	65	61	0.01	59	62	64	62	0.23
Physically active ≥ 1 h/wk, %	11	12	13	17	0.001	10	14	12	17	< 0.001
Obesity,[1] %	48	44	47	41	0.03	47	45	44	44	0.51
Supplement use,[2] %	31	31	30	27	0.12	31	32	32	25	0.005
Medication use,[3] %	25	19	22	22	0.05	25	22	19	22	0.06
Self-reported diabetes, %	2	1	2	2	0.35	1	1	2	2	0.50
Depression,[4] %	12	9	10	10	0.60	11	10	10	9	0.52
Anxiety,[4] %	6	5	5	6	0.001	5	6	5	5	0.12

* Obtained from ANOVA for continuous variables and chi-square for categorical variables. [1] BMI ≥ 30 kg/m^2. [2] Dietary supplements included the intake of iron, calcium, vitamins and other dietary supplements. [3] Medications such as omeprazole and pantoprazole, which reduce the production of acid. [4] Hospital Anxiety and Depression Scale (HADS) scores ≥8 were considered as being anxious or depressed.

group.

Assessment of gastrointestinal reflux disorder To assess functional gastrointestinal disorders, we used the validated Persian version of the ROME III diagnostic criteria [2]. During the face validation of this instrument, we found that most participants were not able to recognize the difference between the descriptors used in ROME III. Therefore, we changed the descriptors in ROME III to a 4-item rating scale (never or rarely, sometimes, often, and always) for each question. We defined GERD as the presence of heartburn sometimes, often, or always during the three months prior to the study [2]. In addition, we asked about the severity of GERD using a 4-item rating scale (mild, moderate, severe, and very severe).

Assessment of other variables

Data on body weight and height were obtained through a self-report questionnaire. Body mass index (BMI) was calculated as weight (kg) divided by height (in meters squared). Obesity was defined as having a BMI of ≥ 25 kg/m2. The general practice physical activity questionnaire (GPAQ) was used to assess physical activity levels of the study participants [16]. Based on this questionnaire, participants were classified as active (≥ 1 h/wk) and inactive (< 1 h/wk). Additional covariates, e.g., age, gender, marital status, educational level, family size, smoking status, disease history, current use of antiacid medications (including proton pump inhibitors such as omeprazole and pantoprazole) and dietary supplements were obtained using self-administered questionnaires. Data on the prevalence of depression and anxiety were collected through the Hospital Anxiety and Depression Scale [17]. Individuals with a score of ≥ 8 were considered as depressed or anxious. Data on diet-related practices including meal regularity, chewing efficiency, intrameal fluid intake, breakfast skipping, frequency of fried food intake, speed of eating, the interval between lunch and afternoon rest were assessed using a pretested self-administered questionnaire. Meal pattern regularity was assessed by asking individuals about the regularity of their meals: “Do you consume your meals regularly?” The participants were able to choose one of these choices: never, sometimes, often, or always. Individuals, who had reported that they were often or always

Table 2: General characteristics of study participants across dietary patterns

	HFLP (n = 228)	HFHP (n = 1453)	LFLP (n = 1453)	LFHP (n = 228)	P*
Age, means ± SD, y	35.7 ± 6.9	36.3 ± 7.9	36.2 ± 7.7	36.9 ± 8.4	0.44
Weight, means ± SD, kg	68.2 ± 13.3	69.1 ± 13.3	68.0 ± 13.0	69.4 ± 12.7	0.11
BMI, means ± SD, kg/m^2	24.8 ± 3.9	24.7 ± 3.7	25.0 ± 3.8	24.9 ± 3.6	0.50
Female, %	58	53	65	52	< 0.001
Married, %	79	82	83	75	0.004
Current smoker, %	18	14	13	13	0.002
Family size ≥ 4, %	13	13	12	14	0.47
University graduate, %	66	63	60	64	0.20
Physically active ≥ 1 h/wk, %	14	15	11	12	0.02
Obesity,[1] %	45	44	46	43	0.64
Supplement use,[2] %	29	28	32	28	0.20
Medication use,[3] %	25	22	23	15	0.02
Self-reported diabetes, %	1	2	2	1	0.29
Depression,[4] %	23	28	29	29	0.52
Anxiety,[4] %	14	12	15	14	0.06

* Obtained from ANOVA for continuous variables and chi-square for categorical variables.
[1] BMI ≥ 30 kg/m^2
[2] Dietary supplements included the intake of iron, calcium, vitamins, and other dietary supplements.
[3] Medications such as omeprazole and pantoprazole, which reduce the production of acid.
[4] Hospital Anxiety and Depression Scale (HADS) scores > 8 were considered as being anxious or depressed.

consumed their meals regularly were defined as having a regular meal pattern. Intrameal fluid intake was assessed through questions about fluid consumption before, within, or after a meal (never, sometimes, often, and always). Meal-to-sleep interval was also evaluated and the participants were classified as having either short (≤ 2 h) or long (> 2 h) meal-to-sleep interval. The frequency of breakfast consumption was asked and skipping breakfast was defined as taking breakfast never or one day per week. Patterns of tea, coffee, and chocolate consumption were also assessed with a validated questionnaire. Those consuming tea and coffee ≥ 2 times a day and chocolate ≥ 5 times a week were considered frequent users of these food items.

Statistical analysis

Statistical analyses were performed using SPSS 18.0 (IBM, Armonk, NY, USA). Continuous variables were examined across different quartiles of fat and protein consumption using one-way ANOVA. We applied the $\chi 2$ test to compare the distribution of participants across different categories of fat and protein intake. Logistic regression analysis was used in different models to examine the association between fat and protein intake and reflux. In the first model, we adjusted our model for age, sex, and energy intake (kcal/d). In the second model, we additionally adjusted for physical activity (as an ordinal variable) and smoking status (nonsmoker, ex-smoker, or current smoker), marital status, family size, education, supplement or medication use, diabetes, depression, and anxiety. We further controlled for dietary behaviors including regular meal intake; the interval between dinner and sleep; the interval between lunches and lying down (< 30 min or > 30 min); breakfast skipping (yes/no); intrameal fluid intake; chewing quality; chocolate, tea, and coffee consumption and soft drinks intake (defined as at least 5 cups per week; yes/no). In the final model, we additionally controlled for BMI (< 25 kg/m2 vs ≥ 25 kg/m2) to see if the associations were independent of obesity. In all analyses, the first category of LFHP was taken as the reference. P trend was obtained for logistic regression analysis using the edian values of each quartile. A p value of less than 0.05 was considered significant.

Results

The study sample consisted of 3362 participants with a mean age of 36.2 ± 7.8 years; 58.3% of participants were women. General characteristics of the study participants across quartiles of fat intake and protein intake are summarized in Table 1. Individuals in the highest quartile of fat intake had a lower mean BMI and were more likely to be male, current smokers, and educated and less likely to use medications and be obese. Individuals in the highest quartile of protein intake had a higher mean weight and age and were less likely to use supplements and be female. There was no significant difference in other variables across quartiles of fat intake and protein intake.

General characteristics of study participants across dietary patterns are presented in Table 2. Individuals following the LFHP diet were less likely to be female, married, current smokers, and physically active and use medications. There was no significant difference in other variables across dietary patterns.

Distribution of participants in terms of dietary

Table 3: Diet-related practices across quartiles of fat and protein intake

	Fat intake					Protein intake				
	Q1	Q2	Q3	Q4	P*	Q1	Q2	Q3	Q4	P*
Meal regularity,[1] %	65	68	71	73	0.003	64	69	72	73	<0.001
Intrameal fluid intake,[2] %	77	75	74	71	0.03	78	75	73	71	0.007
Meal-to-sleep interval,[3] %	34	31	32	31	0.59	33	31	32	32	0.88
Chocolate consumption ≥ 5 times/week, %	11	11	19	22	<0.001	12	14	17	20	<0.001
Tea consumption ≥ 2times/day, (%)	72	79	78	78	0.001	72	78	78	80	0.003
Coffee consumption ≥ 2 times/day, %	11	7	6	8	0.002	10	8	7	8	0.03
Soft drink consumption ≥ 5 times/wk, %	8	7	9	11	0.05	10	7	7	10	0.01
Breakfast skipping,[6] %	8	7	7	7	0.63	9	8	6	6	0.04
Chewing quality,[7] %	15	14	16	12	0.15	16	16	13	12	0.04

* Obtained from chi-square for categorical variables.
[1] Individuals who often or always consumed their meals regularly.
[2] Intrameal fluid intakes were assessed through questions about fluid consumption with meals or immediately before and after meals.
[3] Two classes of study participants regarding the interval between meals and sleeping were identified: short and long meal-to-sleep interval.
[4] Defined as taking breakfast never or one day per week.
[5] People who spent more than 15 minutes to take their main meals

habits across quartiles of fat and protein intakes is summarized in Table 3. Individuals in the highest quartile of fat intake were more likely to have meal regularity and be frequent chocolate, soft drink, and tea consumers and less likely to have high intrameal fluid intake and frequent coffee consumers. Individuals in the highest quartile of protein intake were more likely to have meal regularity and be frequent chocolate and tea consumers and less likely to have high intrameal fluid intake and be frequent coffee consumers. There was no significant difference in other variables across quartiles of fat and protein intakes.

Distribution of the study participants across dietary patterns is presented in Table 4. Individuals with the LFHP diet were more likely to have meal regularity and be frequent coffee consumers and less likely to have intrameal fluid intake and be frequent chocolate and soft drink consumers and breakfast skippers. Distribution of participants in terms of chewing quality was also significantly different across dietary patterns. There was no significant difference in other variables

Table 5 presents the adjusted odds ratios (ORs) for GERD across different quartiles of fat and protein intakes. Dietary fat intakes were not significantly associated with GERD, even after controlling for confounding factors including BMI (OR: 1.11, 95% CI: 0.96-1.78). The same was true for protein intakes, such that those with the highest protein intake did not have a significantly reduced odds for GERD, either before (OR: 0.83, 95% CI: 0.67-1.04) or after adjustment for potential confounders (OR: 0.97, 95% CI: 0.56-1.67) including BMI (OR: 0.84, 95% CI: 0.48-1.47).

Adjusted odds ratios for GERD across dietary patterns are shown in Table 6. Adherence to LFHP diet was not significantly associated with the odds of GERD. Even after adjustment for potential confounders, including diet-related variables, we found no significant association between adherence to LFHP diet and GERD. Additional controlling for BMI did not alter this finding.

Discussion

We found that adherence to the HPLF dietary pattern was not associated with a reduced risk of

Table 4: Diet-related practices across dietary patterns

	HFLP (n = 228)	HFHP (n = 1453)	LFLP (n = 1453)	LFHP (n = 228)	P*
Meal regularity,[1] %	71	72	66	74	0.001
Intrameal fluid intake,[2] %	76	72	77	72	0.01
Meal-to-sleep interval[3] %	28	32	32	32	0.54
Chocolate consumption ≥ 5 times/week, %	26	20	11	11	< 0.001
Tea consumption ≥ 2 times/day, (%)	77	78	75	81	0.07
Coffee consumption ≥ 2 times/day, %	5	7	10	7	0.04
Soft drink consumption ≥ 5 times/wk, %	12	9	8	5	0.03
Breakfast skipping,[4] %	12	6	8	5	0.01
Chewing quality,[5] %	9	14	12	14	0.004

* Obtained from chi-square.
[1] Individuals, who had reported that they were often or always, consumed their meals regularly.
[2] Intrameal fluid intakes were assessed through questions about fluid consumption with meals or immediately before and after meals.
[3] Two classes of study participants regarding the interval between meals and sleeping were identified: short or long meal-to-sleep interval.
[4] Skipping breakfast was defined as taking breakfast never or one day per week
[5] People who spend more than 15 minutes to take their main meals.

Table 5: Adjusted odds ratios and 95% CIs for GERD across different categories of fat and protein intakes[1]

	Quartiles of fat intake					Quartiles of protein intake				
	1	2	3	4	P trend	1	2	3	4	P trend
Crude	1.00	0.94 (0.75-1.18)	0.82 (0.66-1.03)	0.95 (0.76-1.18)	0.42	1.00	0.87 (0.69-1.09)	0.83(0.66-1.04)	0.83 (0.67-1.04)	0.11
Model 1	1.00	1.05 (0.80-1.36)	0.92 (0.66-1.29)	1.11 (0.73-1.70)	0.78	1.00	0.88 (0.67-1.16)	0.82 (0.57-1.17)	0.79 (0.49-1.29)	0.32
Model 2	1.00	1.18 (0.89-1.57)	1.00 (0.70-1.43)	1.22 (0.77-1.92)	0.58	1.00	0.96 (0.71-1.29)	0.88 (0.60-1.29)	0.88 (0.52-1.50)	0.58
Model 3	1.00	1.11 (0.83-1.48)	0.92 (0.64-1.33)	1.19 (0.75-1.89)	0.65	1.00	0.96 (0.71-1.30)	0.90 (0.61-1.34)	0.97 (0.56-1.67)	0.82
Model 4	1.00	1.10 (0.81-1.48)	0.87 (0.59-1.26)	1.11 (0.69-1.78)	0.92	1.00	0.94 (0.69-1.29)	0.82 (0.55-1.23)	0.84 (0.48-1.47)	0.44

[1]Logistic regression was used to obtain ORs and 95% CIs.
Model 1: Adjusted for age, sex, and energy intake.
Model 2: Further adjustments were made for marital status, family size, smoking, education, physical activity, supplement or medication use, diabetes, depression, and anxiety.
Model 3: Additionally controlled for meal regularity, meal-to-sleep interval, breakfast skipping, intrameal fluid intake, chewing quality, and tea, coffee, chocolate, and soft-drink consumption.
Model 4: Further adjusted for BMI.

GERD. This finding remained unaltered even after adjusting for confounding factors. This study is among the first studies examining the association between combined fat and protein intake and the risk of GERD.

GERD is a common disease that affects many people [2]. We found no association between dietary fat intake and GERD. A randomized controlled trial (RCT) on healthy volunteers in Germany found no difference in postprandial lower esophageal sphincter pressure after a high-fat meal [11]. Another RCT in Italy showed that increasing fat intake did not affect reflux for at least three hours after a meal [12]. Findings from a cohort study revealed that high dietary fat intake was not associated with the risk of GERD [10]. However, other studies have found contradictory findings. For example, Fox et al. showed that dietary fat content of meals had an important effect on the frequency of reflux symptoms [4]. A cross-sectional study in the USA suggested that patients with higher fat intakes were more likely to experience reflux than those with a low-fat diet [5]. Doherty et al. showed that patients in the highest quartile of total fat intake had a higher risk of reflux esophagitis [7]. Consumption of high dietary fat was associated with an increased risk of GERD symptoms and erosive esophagitis in another study [5]. Between-study differences might be explained by different study populations, study designs, and instruments used to assess dietary intakes. To reach a conclusive finding, further studies are necessary.

We did not observe any association between dietary protein intake and reflux symptoms. The same finding was also reported from the US, where no significant differences in protein intakes were seen between respondents with and without GERD symptoms [6]. In contrast to our findings, Wu et al. showed that a high intake of protein and calories from protein correlated with a reduced incidence of reflux [13]. Overall, limited information is available linking dietary protein intake to reflux. Further studies are required in this field to reach a conclusion.

Not only did we find no independent associations between fat and protein intakes and GERD, but also we failed to find any significant association between combined fat and protein intakes and GERD. There is no study assessing various patterns of fat and protein intake in relation to the risk of GERD, and our study is the first to examine such an association. However, as GERD was assessed using a questionnaire, rather than clinically, our findings should be considered

Table 6: Adjusted odds ratios and 95% CIs for GERD across dietary patterns[1]

	HFLP (n = 228)	HFHP (n = 1453)	LFLP (n = 1453)	LFHP (n = 228)	P trend
Crude	1	0.93 (0.67-1.30)	1.05 (0.76-1.46)	0.92 (0.60-1.43)	0.21
Model 1	1	0.87 (0.60-1.26)	0.98 (0.68-1.42)	0.99 (0.62-1.55)	0.19
Model 2	1	0.88 (0.59-1.31)	1.00 (0.67-1.48)	1.02 (0.62-1.67)	0.36
Model 3	1	0.92 (0.61-1.39)	1.04 (0.69-1.56)	1.09 (0.66-1.80)	0.27
Model 4	1	0.82 (0.54-1.24)	1.02 (0.68-1.54)	1.04 (0.62-1.74)	0.30

[1] Logistic regression was used to obtain ORs and 95% CIs.

Model 1: Adjusted for age, sex, and energy intake.

Model 2: Further adjustments were made for marital status, family size, smoking, education, physical activity, supplement or medication use, diabetes, depression, and anxiety.

Model 3: Additionally controlled for meal regularity, meal-to-sleep interval, breakfast skipping, intrameal fluid intake, chewing quality, and tea, coffee, chocolate, and soft-drink consumption.

Model 4: Further adjusted for BMI.

preliminary, and additional studies would be needed to shed light on this issue.

There is consistent evidence to support the role of dietary fat in causing temporary episodes of reflux [5]. Several physiological studies of human volunteers have shown an increased frequency of transient lower esophageal sphincter relaxation and increased esophageal acid exposure with higher fat consumption [7]. It has been established that high-fat diets decrease lower esophageal sphincter pressure and delay gastric emptying, which may lead to a greater incidence of reflux [5]. Concerning dietary protein intake, it has been suggested that protein intake might stimulate faster gastric emptying, thereby reducing the risk of GERD [13].

This study has several strengths. One of the main strengths of the current study was the large sample size included in this study. Previous studies have mostly been performed on small sample sizes. The associations we identified are independent of many factors, because of adjustments for several potential confounders. This study has also several potential limitations. First, it has a cross-sectional design, through which no causality can be established [8]. Second, estimates of nutrient intakes based on FFQ are not precise, and there is always the potential for measurement errors [2]; however, the questionnaire we used is one of the most well-validated and commonly used FFQs in the country. In addition, the measure of physical activity was only approximated, and detailed validated questionnaires were not used in the current study. Finally, although we controlled for a wide range of confounders, the effect of residual confounding cannot be excluded.

Conclusion

In conclusion, in this large-scale cross-sectional study in Iranian adults, we failed to find any significant association between adherence to a low-fat, high-protein diet and risk of GERD. However, due to several limitations, further studies are required to be done in this field.

It seems that, in order to achieve a definitive conclusion, more studies with different designs are needed. Future studies should evaluate the effect of the type of fat on reflux disorder.

Conflict of Interests

The authors declare that there is no conflict of interests regarding the publication of this paper.

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