

Association of dietary patterns with migraine: A matched case-control study

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Keywords

Migraine Disorders; Dietary Pattern; Principal Component Analysis; Western Diet; Prudent Diet

Abstract

Background: Little is known about the association between dietary patterns and odds of migraine. We aimed to investigate the association between posteriori dietary patterns and migraine odds and migraine-related outcomes using principal component analysis (PCA).

Methods: A total of 500 participants enrolled in this age- and sex-matched case-control study. Subjects in the case group were migraine patients who were diagnosed by a neurologist (n = 250) and subjects in the control group were healthy individuals (n = 250). Dietary intake was assessed using a 168-item semi-quantitative Food Frequency Questionnaire (FFQ). Extraction of dietary patterns was performed via PCA. Information on the wide range of covariates and

migraine-related outcomes were collected.

Results: The 2 major dietary patterns of the “Western diet” and “prudent diet” were extracted using PCA. Those who were in the highest quartile of the prudent diet had the lowest odds of migraine in the fully adjusted model [odds ratio (OR) = 0.10; 95% confidence interval (CI): 0.04-0.21]. Additionally, higher adherence to the Western diet was positively associated with migraine odds (P < 0.001) and this association remained significant and even increased after adjusting a wide range of confounders. Among migraine sufferers, those who had the highest score on the Western diet, had significantly higher attack frequency compared to the patients in the first quartile (15.4 ± 8.9 vs. 12.3 ± 8.6; P = 0.004).

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Conclusion: The finding of a significant association between the 2 extracted dietary patterns and migraine odds highlights the possible role of diet in both the prevention and stimulation of migraine.

Introduction

Migraine as a primary headache disorder is highly prevalent in the general population with a rising trend and affects 11-18% of individuals worldwide.^{1,2} Moreover, it mostly occurs in people younger than 50 years of age, the most productive years of adulthood, thus causing substantial personal and societal burdens.³⁻⁵ According to the results of the Global Burden of Disease Study 2016 (GBD 2016), migraine was the first cause of disability in those under 50 years of age.⁶ Additionally, migraine is more than a headache disorder since it is also associated with a wide range of comorbidities that reduce quality of life (QOL).⁷

According to the available evidence, migraine can be induced by a wide spectrum of triggers, which provides the opportunity for the management of attacks, and consequently, advancements in the understanding of underlying mechanisms. The most frequently reported triggers include fatigue, fasting, insomnia, stress, odors, sound, light, alcohol consumption, and dietary factors.⁸⁻¹¹ A long list of potential dietary triggers has been reported by migraineurs including processed, salted, fermented foods, monosodium glutamate, dairy products, red wine, citrus fruits, onions, tomatoes, caffeine, chocolate, nuts, and fatty foods.^{8,9,12,13} However, identification of food ingredients as a trigger can be challenging since it depends on the amount of ingested food, timing, presence of some comorbidities, and immunological response.^{14,15} Moreover, eating habit as well as synergistic and interactive effects of different nutrients and food groups is neglected. Therefore, it seems more informative to identify dietary patterns and their association with migraine rather than focus on receiving a particular nutrient or food group.

To date, several studies have looked into the association between diet and migraine.¹⁶⁻²⁶ Although their findings supported the relationship between dietary patterns and migraine-associated outcomes, generally, some limitations should be acknowledged. First, the extracted dietary patterns in some of these researches were based on a 24-hour recall or a pre-prepared checklist of migraine triggers.^{17,18,21} Second, previous research concerning this association mostly focused on a

specific property of diet including micronutrient content,^{22,23} and quality and dietary indices based on a priori scoring method.^{17-20,24-26} A priori methods define patterns using previous knowledge about diet-outcome association while posteriori approaches, such as principal component analysis (PCA), identify sets of dietary patterns attributed to the studied population.²⁷ Third, previous researches have mostly examined the association between dietary patterns and migraine characteristics and there is limited evidence of association between dietary patterns and the odds of migraine itself.

Therefore, the current study was conducted with the aim to investigate whether the dietary patterns extracted through PCA as a posteriori method are associated with the risk of migraine and whether adherence to these major dietary patterns is associated with migraine characteristics. We hypothesized that different dietary patterns were positively or negatively associated with migraine odds and its related outcomes including frequency, severity, and duration of attacks.

Materials and Methods

Study setting: This age- and sex-matched case-control study was conducted in the headache clinic of Sina hospital, Tehran, Iran, between April 2021 and May 2022. The ethical committee of Tehran University of Medical Sciences, Iran, reviewed and approved the study protocol (IR.TUMS.MEDICINE.REC.1399.1287). Participation was voluntary and informed consent was obtained from all subjects.

Selection of cases and controls: We defined a case as a subject aged 18 to 60 years, who was diagnosed with migraine by an expert neurologist according to the International Classification of Headache Disorders-3rd edition (ICHD-III).²⁸ Pregnant/breastfeeding women, patients with acute medical problems, and those suffering from psychotic disorders (that can cause persistent pain) were excluded from the study. A potential control was a person aged 18 to 60 years who had no history of migraine or other headache disorders. Controls were recruited from the outpatient clinic. The reason for selecting the control group from this clinic was to ensure that they do not suffer from diseases that are known to be related to diet. The same exclusion criteria were applied to the controls as to the cases. Additionally, participants with any recent dietary modifications were excluded from the study. For each migraine case, 1 control

individual was included that was matched in terms of sex and frequency matched on 5-year age group. In total, 250 cases and 250 controls were enrolled.

Assessment of covariates and migraine-related outcomes: Data on demographic characteristics, socio-economic status, and health-related behaviors were gathered using a specially designed questionnaire, through a face-to-face interview. From this questionnaire, data were extracted concerning age, gender, occupation (unemployed, employed, homemaker, and retired), educational level (high school, diploma, and college education), marital status (never married, married, divorced, and widowed), smoking (non-smoker, previously a smoker, and smoker), menopause, and average hours of sleep. The International Physical Activity Questionnaire-Short Form (IPAQ-SF) was used to evaluate the physical activity level during the last week.²⁹ Low, moderate, and vigorous activities were defined as metabolic equivalent (MET) of less than 600, between 600-3000, and higher than 3000 METs/min/week, respectively.

According to a standardized protocol, anthropometric measurements including weight and height were measured using calibrated equipment. Participants were weighted to the nearest 0.1 kg and their height was measured using a portable stadiometer to the nearest 0.5 cm, after they were asked to remove their shoes and heavy clothing. Body mass index (BMI) was calculated as the ratio of weight (kg) to the square of height (m).

Participants in the case group were asked about the frequency of attacks per month and the duration of each attack. Migraine severity was evaluated via a visual analog scale (VAS) ranging from 0 to 10, in which 0 meant no pain and 10 the worst imaginable pain. Additionally, data regarding the currently used prophylactic medications were collected.

Dietary assessments: A standardized diet interview was conducted using a validated semi-quantitative Food Frequency Questionnaire (FFQ) for the previous 12 months. The questionnaire was validated previously in Iran. This FFQ included 168 food items with 5 intake frequencies (per day, per week, per month, per year, or never) and quantity (in specified portion size) of consumption. The reported frequency of each food item was then converted to a daily portion intake by multiplying the frequency of each food item by portion size. The intake of energy and nutrients was calculated using Nutritionist 4 software (First Databank Inc., Hearst Corp., San Bruno, CA, USA),

which was modified for Iranian foods.

Dietary pattern analysis: The 168 food items from the FFQ were reduced to 29 food groups based on the similarity of the nutrient content and food triggers of migraine (Table 1). Using varimax rotation, PCA was applied to identify major dietary patterns. We retained 2 factors representing 19.5% of the total variance, determined by the scree plot and eigenvalue (> 1.7). Higher factor loading values represent stronger association between a participant's diet and the dietary pattern. The extracted dietary patterns were named on the basis of food groups that had high positive loading. For each identified factor, a component score was calculated for each participant as the sum of intake of food groups weighed by factor loading. Sample adequacy was checked using the Kaiser-Meyer-Olkin (KMO) test (0.69). Subsequently, dietary pattern scores were categorized into quartiles for further analysis.

Continuous variables were presented as mean and standard deviation (SD) and their difference was examined using the independent sample t-test. Categorical variables were described via proportions and the chi-square test was used to identify significant differences across case and control groups. To investigate the association between adherence to dietary patterns and odds of migraine compared to the control group, we performed a logistic regression analysis. The odds ratio (OR) and 95% confidence interval (CI) were calculated for the quartiles of PCA dietary patterns in crude and adjusted models. The first model was adjusted for age, gender, BMI, and total calorie intake. The second model was further adjusted for marriage, occupation, education, and menopause. Finally, sleep hours, activity scores, smoking and prophylactic medications were further considered in the fully adjusted model. ANOVA was used to explore the difference in migraine characteristics across quartiles of extracted dietary patterns. All P-values of less than 0.05 were considered statistically significant in all analyses. All analyses were performed via SPSS software (version 22, IBM Corp., Armonk, NY, USA).

Results

Characteristics of the study populations: The demographic, lifestyle, and clinical characteristics of the study population are presented in table 2. A total of 500 participants enrolled in this age- and sex-matched case-control study (250 subjects in each group), 82.8% of whom were women.

Table 1. Food groups used for dietary pattern analysis

| Food groups | Food items |
|--------------------|---|
| Eggs | Egg |
| Fish | All types of fish, canned tuna |
| Legumes | Different kinds of beans, peas, and lentil |
| Soya | Soybean |
| Fruits | All kinds of fresh fruits, dry fruits, natural fruit juice, fruit conserves |
| Citrus fruits | Orange, tangerine, grapefruit, sweet lemon, sour lemon |
| Fruit juice | All fruit juices |
| Starchy vegetables | Potato, corn |
| Leafy vegetables | All leafy vegetables |
| Other vegetables | Other vegetables |
| Garlic/onion | Garlic, onion |
| Processed meat | Sausages and burgers |
| Red meat | Beef and lamb |
| Poultry | Chicken |
| Organ meat | all types of organ meat |
| Soft drinks | Cola |
| Nuts | Walnuts, peanuts, hazelnuts, pistachio, almonds, seeds |
| Vegetable pickles | All types of vegetable pickles |
| Solid oils | Hydrogenated vegetable oil, animal oil, margarine, butter, mayonnaise |
| Vegetable oils | Liquid oils, olive and olive oil |
| Sweets | Pastries, sugar, jam, honey, candy, cake, and biscuits |
| Coffee group | Coffee and chocolate |
| High-fat Dairy | All types of high-fat milk, yogurt, ice cream |
| Low-fat dairy | All types of low-fat milk, yogurt, ice cream, dough, curd, cheese |
| Cheese | Cheese |
| Whole grains | Dark Iranian bread, barely |
| Refined grains | White bread including lavash, baguette, rice, pasta, vermicelli |
| Seasoning | Black pepper, ketchup, lime juice |
| Fast food/ snacks | Pizza, potato chips, French fries |

The mean age of the participants was 37.7 years. Compared to the control group, migraine patients had a higher average of sleep hours ($P < 0.001$) and lower calorie intake/day ($P < 0.001$). In addition, there was a significant difference between the two groups regarding physical activity, education, and occupation. However, no statistically significant difference was found between the groups in terms of smoking, BMI, menopause, and marriage status.

The information regarding the clinical characteristics of subjects in the case group is also presented in table 2. The presence of aura was diagnosed in 12% of migraine patients. The mean frequency of migraine attacks/month was 12.3 with a mean severity of 7.6 and a mean duration of 24.2 hours. Among the migraine patients included in the study, about 17% used tricyclic antidepressants (TCAs), 15% propranolol, 9% topiramate, and 6% sodium valproate.

Dietary patterns: Component factor loadings of the 29 food groups for the two dietary patterns extracted through PCA are presented in table 3. A high positive factor loading shows a strong

association between predictors (food groups) and extracted dietary patterns, while a negative factor loading value indicates an inverse relationship.

The first factor from the PCA, labeled prudent diet, was characterized by a high intake of vegetables, citrus fruits, garlic/onion, low-fat dairy, seasoning, fruits, legumes, cheese, fish, soya, poultry, and vegetable oils. The second PCA-derived factor, labeled the Western diet, had high intakes of sweets, processed meat, fast food/snacks, soft drinks, fruit juice, organ meats, high-fat dairy, refined grains, coffee group, whole grains, nuts, pickles, egg, red meat, and solid oils. These two dietary patterns explained 19.5% of the total variation in dietary intake.

Association between dietary patterns and odds of migraine vs. control: Table 4 shows the chance of having migraine across quartiles of dietary patterns. In the unadjusted model, there was a significant negative association between adherence to the prudent diet and odds of migraine throughout all categories compared to the first quartile ($P < 0.001$).

Table 2. Mean scores of questionnaires and frequency of categorical questions

| Variable | Migraine (250) | Control (250) | P |
|------------------------------|----------------|-----------------|---------|
| Gender | | | |
| Female | 207 (82.8) | 207 (82.8) | > 0.999 |
| Male | 43 (17.2) | 43 (17.2) | |
| Age (year) | 37.5 ± 10.5 | 37.9 ± 10.1 | 0.610 |
| BMI (kg/m ²) | 25.8 ± 5.1 | 26.5 ± 4.4 | 0.090 |
| Sleep (hours) | 7.1 ± 1.4 | 6.5 ± 1.2 | < 0.001 |
| Calorie intake (Kcal/day) | 2211.0 ± 663.0 | 2560.0 ± 1291.0 | < 0.001 |
| Menopause | 37 (17.8) | 41 (19.8) | 0.930 |
| Physical activity | | | |
| Low | 159 (68.5) | 107 (42.8) | < 0.001 |
| Moderate | 56 (24.1) | 142 (56.8) | |
| High | 17 (7.3) | 1 (0.4) | |
| Education | | | |
| Illiterate | 0 (0) | 3 (1.2) | < 0.001 |
| High school | 27 (10.8) | 43 (17.2) | |
| Diploma | 60 (24.0) | 89 (35.6) | |
| College education | 163 (65.2) | 115 (46.0) | |
| Occupation | | | |
| Unemployed | 126 (50.4) | 83 (33.2) | < 0.001 |
| Employed | 90 (36.0) | 132 (52.8) | |
| Homemaker | 9 (3.6) | 14 (5.6) | |
| Retired | 25 (10.0) | 21 (8.4) | |
| Marriage status | | | |
| Never married | 70 (28.0) | 60 (24.0) | 0.340 |
| Married | 165 (66.0) | 178 (71.2) | |
| Divorced | 13 (5.2) | 12 (4.8) | |
| Widowed | 2 (0.8) | 0 (0) | |
| Smoking | | | |
| Non-smoker | 229 (92.0) | 234 (93.6) | 0.770 |
| Previously smoker | 6 (2.4) | 5 (2.0) | |
| Smoker | 14 (5.6) | 11 (4.4) | |
| Clinical characteristics | | | |
| Migraine type | | | |
| Migraine with aura | 30 (12.0) | - | |
| Migraine without aura | 220 (88.0) | - | |
| Prophylactic Medications | | | |
| Sodium valproate | 15 (6.0) | - | |
| TCAs | 43 (17.2) | - | |
| Topiramate | 22 (8.8) | - | |
| Propranolol | 39 (15.6) | - | |
| Frequency of attacks (month) | 12.3 ± 8.6 | - | |
| Severity of attacks (VAS) | 7.6 ± 6.0 | - | |
| Duration of attacks (hours) | 24.2 ± 22.8 | - | |

Data are presented as mean ± standard deviation (SD) for continuous measures, and n (%) for categorical measures.

P value from chi-square test for categorical variables and independent sample t-test for continuous variables P values < 0.05 are in bold.

BMI: Body mass index; TCAs: Tricyclic antidepressants; VAS: Visual analog scale

This association remained significant even in the fully adjusted model after considering age, gender, BMI, total calorie intake, marriage, occupation, education, menopause, sleep hours, activity scores, smoking, and prophylactic medications. Those who were in the highest quartile of the prudent diet had the lowest odds of

migraine compared to the control group (OR = 0.10; 95% CI: 0.04-0.21).

In the case of the Western dietary pattern, in the crude model, there was a significant positive association between the third and fourth quartile of the Western diet and migraine odds (Q3: OR = 2.71; 95% CI: 1.61-4.54; Q4: OR = 2.45; 95% CI: 1.46-4.09).

Table 3. Factor loadings and explained variation of dietary patterns

| Food groups | Prudent diet | Western diet |
|--------------------|--------------|--------------|
| Leafy vegetables | 0.75 | |
| Other vegetables | 0.72 | |
| Citrus fruits | 0.56 | 0.17 |
| Garlic/onion | 0.49 | |
| Low-fat dairy | 0.49 | 0.16 |
| Seasoning | 0.47 | |
| Starchy vegetables | 0.44 | 0.32 |
| Fruits | 0.39 | 0.33 |
| Legumes | 0.35 | |
| Cheese | 0.34 | |
| Fish | 0.34 | |
| Soya | 0.28 | |
| Poultry | 0.15 | |
| Vegetable oils | 0.14 | |
| Sweets | | 0.56 |
| Processed meat | | 0.52 |
| Fast food/snacks | -0.13 | 0.49 |
| Soft drinks | | 0.43 |
| Fruit juice | 0.32 | 0.42 |
| Organ meat | | 0.41 |
| High-fat dairy | 0.17 | 0.40 |
| Refined grains | | 0.38 |
| Coffee group | | 0.28 |
| Whole grains | 0.10 | 0.28 |
| Nuts | | 0.27 |
| Pickles | | 0.25 |
| Egg | 0.18 | 0.23 |
| Red meat | | 0.21 |
| Solid oils | 0.19 | 0.20 |

Values < 0.1 were excluded for simplicity.

In the fully adjusted model, ORs were still significant in the top two quartiles and even increased (Q3: OR = 4.43; 95% CI: 2.19-8.97; Q4: OR = 3.47; 95% CI: 1.70-7.06; P < 0.001).

Association between dietary patterns and migraine characteristics: Table 5 indicates migraine characteristics across quartiles of the two extracted dietary patterns. Participants with the

highest scores on the Western diet (Q4) had significantly higher attack frequency compared to the first quartile (15.4 ± 8.9 vs. 12.3 ± 8.6; P = 0.004). There was no significant difference between the quartiles of either the prudent diet or the Western diet regarding the severity and duration of attacks.

Discussion

Our findings in this case-control study suggest that adherence to a dietary pattern mostly consisting of high amounts of vegetables, fruits, low-fat dairy, cheese, legumes, and fish (labeled as the prudent diet) is associated with lower odds of migraine compared to the control group. However, higher adherence to the Western diet (which consisted of a high intake of sweets, processed meat, fast food/snacks, soft drink, fruit juice, organ meat, high-fat dairy, and refined grains) was positively associated with migraine risk. Moreover, among migraine sufferers, those who had the highest score in the Western diet had significantly higher attack frequency compared to patients in the first quartile.

Finding the two major dietary patterns of Western and prudent diet among migraine sufferers in our study was in line with the findings of Hajjarzadeh et al., who also extracted two dietary patterns among 285 volunteer women with migraine, the “healthy pattern” (identified by high intake of fruits, fish, vegetable pickles, vegetables, and legumes) and the “Western pattern” (identified by high intake of cola, salted nuts, processed meat, and fast foods and snacks).¹⁶ In addition, in agreement with our findings, they found that migraine patients with high adherence to the Western dietary pattern had higher attack frequency.¹⁶ However, they also revealed that migraineurs with high adherence to the healthy dietary pattern had lower attack frequency.

Table 4. Odds ratios (OR) and 95% confidence interval (CI) for the association between adherence to dietary patterns and migraine odds

| Patterns | | Q1 (n = 123) | Q2 (n = 123) | Q3 (n = 123) | Q4 (n = 123) | P |
|--------------|---------|--------------|------------------|------------------|------------------|---------|
| Prudent diet | Crude | 1.00 | 0.29 (0.17-0.51) | 0.36 (0.21-0.62) | 0.10 (0.06-0.19) | < 0.001 |
| | Model 1 | 1.00 | 0.30 (0.17-0.53) | 0.39 (0.22-0.69) | 0.12 (0.06-0.22) | < 0.001 |
| | Model 2 | 1.00 | 0.28 (0.15-0.49) | 0.34 (0.19-0.60) | 0.10 (0.05-0.19) | < 0.001 |
| | Model 3 | 1.00 | 0.29 (0.14-0.58) | 0.45 (0.23-0.90) | 0.10 (0.04-0.21) | < 0.001 |
| Western diet | Crude | 1.00 | 1.65 (0.99-2.75) | 2.71 (1.61-4.54) | 2.45 (1.46-4.09) | 0.001* |
| | Model 1 | 1.00 | 1.89 (1.11-3.21) | 3.82 (2.18-6.69) | 3.54 (2.00-6.28) | < 0.001 |
| | Model 2 | 1.00 | 1.89 (1.09-3.29) | 4.25 (2.37-7.62) | 3.73 (2.06-6.74) | < 0.001 |
| | Model 3 | 1.00 | 1.75 (0.87-3.50) | 4.43 (2.19-8.97) | 3.47 (1.70-7.06) | < 0.001 |

*P < 0.05

Model 1 was adjusted for age, gender, BMI, and total calorie intake.

Model 2 was additionally adjusted for marriage, occupation, education, and menopause.

Model 3 was additionally adjusted for sleep hours, activity scores, smoking, and prophylactic medications.

Table 5. Migraine characteristics across quartiles of the two extracted dietary patterns

| Migraine characteristics | Patterns | | | | P |
|--------------------------|--------------|--------------|--------------|--------------|-------|
| | Q1 (n = 123) | Q2 (n = 123) | Q3 (n = 123) | Q4 (n = 123) | |
| | Prudent diet | | | | |
| Frequency attack/month | 12.7 ± 8.8 | 12.1 ± 9.7 | 12.6 ± 8.1 | 11.3 ± 7.3 | 0.870 |
| Severity (VAS) | 7.2 ± 2.2 | 7.2 ± 1.9 | 8.6 ± 11.4 | 7.5 ± 1.7 | 0.510 |
| Duration (hours) | 20.6 ± 21.6 | 29.2 ± 23.1 | 27.3 ± 24.6 | 19.2 ± 21.1 | 0.080 |
| | Western diet | | | | |
| Frequency attack/month | 12.3 ± 8.6 | 10.3 ± 7.6 | 11.1 ± 8.6 | 15.4 ± 8.9 | 0.004 |
| Severity (VAS) | 7.1 ± 1.8 | 8.7 ± 11.9 | 7.2 ± 1.9 | 7.5 ± 1.9 | 0.510 |
| Duration (hours) | 24.9 ± 23.7 | 27.6 ± 24.8 | 27.0 ± 24.1 | 19.0 ± 19.3 | 0.160 |

Data are presented as mean ± standard deviation (SD). P value from ANOVA.

VAS: Visual analog scale

Nevertheless, we could not detect any differences across quartiles of prudent diet scores and attack frequency. This discrepancy could be partially explained by some differences between the food items of the “healthy diet” and “prudent diet” and the interactions of these food groups in the dietary pattern.

In contrast to previous researches, which examined the dietary pattern of migraine patients related to the migraine characteristics using a cross-sectional design, we focused on the association between major dietary patterns and odds of migraine compared to a control group via an age- and sex-matched case-control design. Following the prudent diet even in the second quartile was significantly associated with lower odds of migraine. This finding can emphasize the importance of having a healthy diet in the prevention of migraine. The protective effect of the prudent diet against migraine in our study could be attributed to the high amount of some beneficial micronutrients in this diet. The prudent diet in our study was characterized by a high intake of vegetables and fruits which are considered rich sources of the B vitamins group and magnesium. There is promising evidence from interventional studies supporting the role of these micronutrients in the prevention and alleviation of migraine.³⁰⁻³² Moreover, components of the prudent diet in the current study have low amounts of fats and high amounts of anti-oxidants which have been previously shown to be associated with migraine.³³⁻³⁵

Moreover, our findings indicated that after considering a wide range of confounders, the higher quartiles of the Western diet were associated with about three to four-fold increase in the odds of having migraine compared to the control group. The positive association between the Western diet and odds of migraine could be

partially due to the effect of this diet on body weight.^{36,37} The majority of its food items have high-fat content and can have a role in the development of obesity.³⁷ The findings of previous studies support the relationship between obesity and migraine risk, and it has been proposed as a risk factor for migraine chronification.³⁸⁻⁴¹ However, the mean BMI of both study groups in our study was in the overweight range and the significant association between the Western diet and migraine remained unchanged even after adjustment for BMI. Therefore, it seems that the relationship between the Western diet and odds of migraine could be beyond body weight differences and another mechanistic pathway may be involved. Recent insights have focused on the neurogenic inflammation hypothesis as an important theory of migraine pathophysiology emphasizing the release of inflammatory agents and their consequent effect on the activation and sensitization of nociceptors.^{42,43} In addition, there is mounting evidence pointing to the abnormal levels of inflammatory mediators in the systemic circulation of migraine patients compared to healthy controls.⁴⁴⁻⁴⁷ Furthermore, diet has a well-known impact on inflammatory status.^{48,49} Accumulating evidence indicates that high intake of refined carbohydrates, omega-6 to omega-3 ratio, and low intake of dietary fiber, have a strong relationship with the production of pro-inflammatory mediators.⁵⁰⁻⁵² Trans fatty acids, which are found in fried and processed foods, can also lead to inflammation.⁵³ It should also be noted that high consumption of sweets and high glycemic load foods and the consequent acute hyperglycemia can contribute to the production of inflammatory mediators such as interleukins (ILs) and tumor necrosis factor alpha (TNF-alpha) through activating nuclear factor kappa beta.^{54,55} All of the mentioned food items are components of

a typical Western diet. Therefore, the Western diet can provoke inflammation by various mechanisms and this hypothesis was further supported by finding a relationship between adherence to the Western dietary pattern and a higher concentration of inflammatory markers including c-reactive protein and IL-6.⁵⁶ Considering the role of inflammation in triggering migraine attacks and the effect of following a Western diet on the inflammatory status, we can hypothesize that adherence to this dietary pattern can contribute to migraine attacks through an inflammatory cascade. Aligned with this evidence, previous research seeking the association between inflammatory properties of diet and migraine characteristics indicated a direct association between headache frequency and dietary inflammatory index.^{24,26}

The present study has some strengths and limitations that should be acknowledged. For the current research, we investigated the whole diet instead of only some triggers and extracted dietary patterns using PCA method, migraine diagnosis was performed by an expert neurologist, and this was among the first case-control studies that investigated the association between dietary pattern and migraine odds. The limitations of our study include its observational design which limits the proving of causal relationship and the existence of some residual confounders that we did not consider in our analysis. However, we evaluated a wide range of confounders including demographic, anthropometric, lifestyle, and clinical, and adjust their effects in the analysis models. In addition, some of the prophylactic

drugs consumed by migraine patients can affect weight and appetite. However, for the current study, we collected data regarding the consumption of these medications and adjusted their effects in the analytical models. Finally, applying FFQ for the assessment of dietary intakes, regardless of its benefit, might have a risk of recall bias because of its retrospective nature.

Conclusion

Our findings suggest that the risk of migraine was positively higher among those who were in the top quartile of the Western diet (mostly consisted of a high intake of sweets, processed meat, fast food/snacks, soft drinks, fruit juice, organ meat, high-fat dairy, and refined grains). In addition, adherence to the prudent diet (consisting of high amounts of vegetables, fruits, low-fat dairy, cheese, legumes, and fish) was associated with lower odds of migraine. The highest quartile of the Western diet was also associated with higher attack frequency among the migraine population. Clearly, further prospective studies are needed to more firmly establish the association between dietary patterns and migraine risk.

Conflict of Interests

The authors declare no conflict of interest in this study.

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