Original Article

Journal of Iranian Medical Council, Volume 4, Issue no. 1
http://dx.doi.org/10.18502/jimc.v4i1.5737

Association of Plant-Based Dietary Patterns with Migraine Headache Severity and Duration among Women

Moein Askarpour[1,2], Ali Sheikhi[1], Faezeh Khorsha[1], Leila Setayesh[1], Mansoureh Togha[3, 4] and Khadijeh Mirzaei[1*]

1. Department of Community Nutrition, School of Nutritional Sciences and Dietetics, Tehran University of Medical Sciences (TUMS), Tehran, Iran

2. Students' Scientific Research Center (SSRC), Tehran University of Medical Sciences (TUMS), Tehran, Iran

3. Department of Neurology, Sina Hospital, Tehran University of Medical Sciences, Tehran, Iran

4. Headache Department, Iranian Center of Neurological Research, Tehran, Iran

*** Corresponding author**

Khadijeh Mirzaei, PhD
Department of Community Nutrition, School of Nutritional Sciences and Dietetics, Tehran University of Medical Sciences (TUMS), Tehran, Iran
Email: mirzaei_kh@tums.ac.ir
mina_mirzaei101@yahoo.com

Received: Oct 4 2020
Accepted: Dec 10 2020

Citation to this article:

Askarpour M, Sheikhi A, Khorsha F, Setayesh L, Togha M, MirzaeiKh. Association of Plant-Based Dietary Patterns with Migraine Headache Severity and Duration among Women. *J Iran Med Counc*. 2021; 4(1):12-24.

Abstract

Background: Migraine is a recurrent disorder which can cause socio-economic and public health burdens. Many factors, especially dietary factors are suggested to induce migraine headaches. The aim of this study was to examine the association between plant-based dietary patterns and headache severity and duration among migraine patients.

Methods: A sample of two hundred and sixty-six women with migraine (18-50 years) took part in the present cross-sectional study. Dietary intake data was collected using a validated and reliable food-frequency questionnaire. Three dietary indices were evaluated including an overall plant-based diet (PDI), healthful Plant-based diet (hPDI), and unhealthful plant-based diet (uPDI). Anthropometric measurements, headache duration, Migraine Disability Assessment (MIDAS), and Visual Analog Scale (VAS) were assessed for all cases. Multinomial logistic regression and linear regression models were used to show the association between headaches and plant-based dietary patterns.

Results: An inverse association between higher adherence to hPDI and severity of headaches was found based on VAS (OR=0.40; 95% CI: 0.21, 0.74; p=0.003), and severe disability based on MIDAS (OR=0.50; 95% CI: 0.26, 0.95; p=0.03). Conversely, uPDI scores were positively associated with severe headaches (OR=3.00; 95% CI: 1.72, 5.23; p<0.001), and disability (OR=2.50; 95% CI: 1.39, 4.51; p=0.001). Moreover, headaches duration showed an inverse significant association with hPDI scores (β=-0.21, 95% CI=-4.69, -1.08, p=0.002).

Conclusion: Plant-based diet, particularly healthful plant foods, was inversely associated with lower severity, disability and duration of headaches. In addition, unhealthy plant foods were associated with higher risk of migraine headaches.

Keywords: Diet, Female, Migraine headache, Vegetarian

Introduction

Migraine is a neurologic disorder characterized by attacks of severe, throbbing headaches with associated features such as photophobia, phonophobia, nausea, and vomiting (1). Migraine, affecting as much as 10% of the global population (2), is considered the first cause of disability in under 50 *s* (3). It greatly affects the quality of life and could even be a huge economic burden (4). Though the exact pathology of the disease is not fully comprehended, but disorders of the central nervous system and immune system, as well as inflammation, genetics, and vascular ischemia have all been proposed as possible contributors to migraine (5). Certain drugs have been introduced to control and manage this disease (6), but due to the major side effects that they could create (7), modification in lifestyle should be the primary approach for managing migraine. The predisposing factors including nutrition may affect the duration and severity of migraine attacks. According to previous studies, tyramine rich foods such as processed meat, cheese, and smoked fish are some of strong migraine triggers (8). On the other hand, it was reported that higher consumption of fruits, vegetables, legumes and nuts is related to reduced headache duration and intensity (9).

Assessing overall diet quality, compared with focusing on single nutrients or foods, may provide better insight into the disease. Plant based dietary pattern which emphasizes on consumption of plant-derived food sources and limited consumption of animal sources, has gained significant attention due to its effect on control and management of chronic diseases (10-12). Moreover, plant-based foods contain certain food nutrients such as riboflavin, magnesium, coenzyme Q10, alpha-lipoic acid, and eicosapentaenoic acid which are shown to play a significant role in reducing the intensity and frequency of migraines (13). On the other hand, refined grains, starches, and sugar-sweetened beverages can also be characterized as plant-based foods, which have been long known to have adverse effects on human health (14). Plus, refined grains such as rice and variety of breads are among the major food staples among Iranians (15). Therefore, three established plant-based diet indexes were used in this study including overall plant-based diet index (PDI), healthful plant-based diet index (hPDI), and unhealthful plant-based diet index (uPDI) to score animal foods, healthy plant foods, and less-healthy plant foods (11). No study has ever investigated the association between plant-based dietary patterns with risk of migraine headaches. Therefore, this cross-sectional observational study was conducted to examine a hypothesized association between plant-based dietary patterns and intensity and duration of migraine headaches.

Materials and Methods

Participants

The present study was conducted as an attempt to improve the Reporting of Observational Studies in Epidemiology. In this cross-sectional study, 266 females aged 18-50 years suffering from migraine headaches were chosen from two neurology clinics in Tehran. Inclusion criteria in the present study were premenopausal women with history of migraine headache who were diagnosed by an experienced neurologist, voluntary participation in the study, Body Mass Index (BMI) between 18.5 and 30, and the first neurology clinic visit. Participants were excluded from the study if they were pregnant or lactating, on specific diets, or their daily energy intakes were lower than 800 *kcal/day* or higher than 4,200 *kcal/day* (n=28). Moreover, women with chronic diseases such as diabetes, cardiovascular diseases, and cancer were excluded. Health status history and amount of medication usage among individuals were checked *via* electronic medical record system.

Assessment of dietary intakes and plant-based dietary indices

Dietary intake was examined using a 147-items semi-quantitative Food Frequency Questionnaire (FFQ), with approved reliability and validity (16). Dietitians filled participants FFQs during a face- to-face interview. The US Department of Agriculture (USDA) Food Composition Tables (FCT) were used to assess nutrients and energy of dietary intake due to limited data on Iranian FCT. Then, nutrient intakes were analyzed using Nutritionist IV software. To compute the plant-based dietary pattern, the method mentioned by Satija *et al* was applied (17). To derive the 3 plant-based diet indices including overall plant-based diet index (PDI), healthful PDI (hPDI), and

unhealthful PDI (uPDI), according to the similarity of nutrients composition, food items were categorized into 18 groups. The food items were categorized in three main groups of animal, healthy, and unhealthy plant-based foods. Healthy plant foods included whole grains, vegetables, fruits, legumes, nuts, vegetable oils, tea and coffee, while fruit juices, sugar-sweetened beverages, refined grains, sweets and desserts, and potatoes were considered as less healthy or unhealthy plant foods. Moreover, dairy, animal fat, egg, meat, fish and seafood, and miscellaneous animal-based foods were considered as animal food items. Then, the food items were transformed to deciles and each item was given a score of 1-10.

To calculate PDI, individuals at the highest and lowest deciles of plant food consumption were given scores of 10 and 1, respectively. Further, participants in the top and bottom deciles of animal foods consumption were given scores of 1 and 10, respectively.

For hPDI, scores of 10 and 1 were used to score study population with the highest and lowest intake of healthy plant foods, respectively. In addition, consumption of unhealthy plant foods and animal food items were given a score of 1 for the highest intake and 10 for the lowest intake.

To assess uPDI, scores of 10 and 1 were given to the highest and the lowest consumption of unhealthy plant foods. In addition, both animal foods and healthy plant foods with the highest to lowest consumption were given a score between 1 and 10.

Finally, these scores were summed to compute three plant-based diet indices with theoretical score ranging from 18 to 180 for three indices. Higher adherence to the three dietary patterns indicated higher total scores for each index.

Migraine diagnosis

In the present study, an experienced neurologist diagnosed episodic migraine, according to International Classification of Headache Disorders 3rd edition (ICHD3) (18). Criteria for migraine diagnosis comprise two types of migraine with aura (MA) and without aura (MO). The diagnosis of MO was based on pre-determined criteria of International Headache Society (IHS); first, the presence of at least two of the following characteristics was the sign for the disease: (a) pulsating quality, (b) unilateral headaches, (c) headaches worsened by physical activity, and (d) moderate or severe pain. Second, at least five attacks fulfilling the following criteria were the next signs: (a) the headache duration lasting from 4 to 72 hours; and (b) the presence of one or more of the following criteria during headache attack including photophobia (sensitivity to light) and/or phonophobia (sensitivity to sound), nausea, and/or vomiting.

In addition, aura is described as a group of symptoms mainly applied as a warning sign that headache is coming (19). MA, based on IHS criteria, is a condition in which more than two headache attacks meet the following criteria: (a) the presence of at least one disorder in sensory, motor, retinal, visual, brainstem, speech or language function; (b) symptom duration of five or more than five minutes, consecutive presentation of two or more symptoms, occurrence of one or more unilateral symptoms, and occurrence of symptoms with headache.

MIDAS and Visual Analog Scale (VAS) questionnaires

To examine headache-related disability, the Migraine Disability Assessment (MIDAS) questionnaire was used. MIDAS questionnaire's validity and reliability were already evaluated in Iranian population (20). Five questions were asked from participants to assess the number of days in the past 3 months in which their performance dropped because of migraine. After that, based on their overall scores, participants were divided into 4 levels of I (0-5, little or no disability), II (6-10, mild disability), III (11-20, moderate disability), and IV (more than 20, severe disability) (21). In addition, VAS questionnaire was applied to evaluate headache pain. VAS included a 10 cm horizontal line and the patient's pain intensity was represented by a point between the extremes. The VAS score cut-off points ranged from 1 to 10 and classified pain in three levels of1 to 3 (mild pain), 4 to 7 (moderate pain), and 8 to 10 (severe pain) (22).

Assessment of other variables

Weight was measured by a digital scale (SECA, Hamburg, Germany) to the nearest 0.1 *kg*, while wearing no shoes and one layer of clothing. Height, by a wall-mounted stadiometer, was recorded to the nearest

0.5 *cm*, while the shoulders were relaxed in standing position with shoes removed. BMI was computed based on the following formula: "weight (*kg*)/height^2 (m^2)". By giving all participants a questionnaire, some characteristics including age, medicine consumption (yes/no), marital status (married, single), family history of migraine (yes/no), specific diet, sensitivity to light or sound (yes/no), education status (≤diploma or >diploma), supplement use (yes/no), and chronic disease history (yes/no) were assessed. To obtain duration and attack onset of headaches after each migraine attack, all participants were given a 30-day headache diary. If the individuals had any problems in fulfilling their diaries, professional neurologists came to give instructions to participants and resolved their problems. To assess Physical Activity (PA), International Physical Activity Questionnaire (IPAC) was used. Activity levels were classified into low, moderate, and high as described by the IPAQ scoring protocol (23). PA was shown as metabolic equivalent hours per week (METs *h*/week).

Ethical code

The present study protocol was confirmed (Ethics code: IR.TUMS.REC.1394.2141) by the research committee of the School of Nutritional Sciences and Dietetics of Tehran University of Medical Sciences (TUMS). All of the participants were asked to sign consent forms.

Statistical analyses

To attain descriptive characteristics of the participants, the chi-square test and one-way analysis of variance (ANOVA) were used. The chi-square test was applied to determine the association between PDI, hPDI, and uPDI and qualitative variables. Quantitative data were normally distributed. One-way analysis of variance (ANOVA) was applied to determine the relationship between PDI, hPDI, and uPDI and quantitative variables. In addition, analysis of covariance (ANCOVA) was applied to compare the dietary intakes of participants among tertiles of PDI, hPDI, and uPDI by adjusting the effect of age, BMI, PA, supplement use, medication consumption, sensitivity to light or sound and energy intake. To assess the association between plant-based dietary indices and the headache severity and disability (VAS tertiles and MIDAS quartiles), multinomial logistic regression was applied in crude and adjusted models. Moreover, to determine the association between headache duration (Dependent variable) and the tertiles of PDI, hPDI, and uPDI (Independent variables), linear regression was used, in crude and adjusted models. The level of statistical significance was considered as $p<0.05$. SPSS statistics version 22.0 (IBM Inc, New York, USA) was used to perform statistical analysis.

Results

Study population characteristics

The baseline characteristics of the participants among tertiles of PDI, hPDI, and uPDI are presented in table 1. The mean (±SD) age, height, weight, BMI, PA, and headache duration of participants were 34.32 (7.86) years, 161.87 (5.14) *cm*, 69.41 (13.02) *kg*, 26.50 (4.88) kg/m^2, 407.73 (519.13) MET/Min/week, 10.03 (10.78) hours, respectively. Quantitative and qualitative variables across PDI, hPDI, and uPDI tertiles did not show any significant differences. However, headache duration showed a statistically significant difference across plant-based diet indices ($p<0.05$), with a descending trend from the lowest to the highest tertiles of PDI, hPDI, and an ascending trend in uPDI. Based on the report of our participants, dietary factors were eliminated from the diet of 83.97% in whom the dietary intake could aggravate their headache severity. Moreover, the percentage of participants who experienced both severe pain and disability based on VAS and MIDAS scores across the lowest (T1) and highest (T3) tertiles of PDI, hPDI, and uPDI were 35.9 *vs.* 31.4, 47.1 *vs.* 28, and 17.9 *vs.* 47.1, respectively. In addition, the percentage of participants with both mild pain and without a disability is indicated in figure 1.

Dietary intake and plant-based diet indices

Nutrient and food intakes of the participants among PDI, hPDI, and uPDI tertiles are presented in table 2. Participants in the top tertile of PDI had higher consumption of fiber, Polyunsaturated Fatty Acid (PUFA), vitamin A, C, B6, folic acid, magnesium, potassium, whole grains, fruit, vegetables, nuts, legumes, tea/coffee, vegetable oils, sugar-sweetened beverages, potatoes, fruit juice, and lower consumption of fat, Saturated Fatty Acid (SFA), Monounsaturated

Table 1. General characteristics of participants across the tertiles (T) of PDI, hPDI, and uPDI

			PDI		p value		hPDI		p value		uPDI		p value
	Total (N=266)	T1 ≤94 (N=89)	T2 95-104 (N=91)	T3 ≥105 (N=86)		T1 ≤89 (N=91)	T2 90-111 (N=88)	T3 ≥112 (N=87)		T1 ≤96 (N=86)	T2 97-106 (N=96)	T3 ≥107 (N=84)	
Quantitative variables													
Age (Year)	34.32 ±7.86	34.25 ±8.08	34.48 ±8.03	34.21 ±7.52	0.96	33.65 ±8.12	33.94 ±7.41	35.39 ±7.99	0.29	34.85 ±7.87	34.16 ±8.0	33.95 ±7.73	0.73
Height (cm)	161.87 ±5.14	161.33 ±5.30	162.70 ±4.91	161.55 ±5.16	0.15	161.58 ±4.88	161.72 ±5.30	162.32 ±5.27	0.59	162.64 ±4.99	161.53 ±5.16	161.46 ±5.23	0.23
Weight (kg)	69.41 ±13.02	69.08 ±12.52	70.52 ±13.14	68.57 ±13.47	0.58	68.57 ±14.58	69.60 ±12.84	70.10 ±11.48	0.72	68.70 ±11.58	70.06 ±12.99	69.39 ±14.49	0.78
BMI (kg/m^2)	26.50 ±4.88	26.53 ±4.56	26.66 ±5.01	26.29 ±5.10	0.87	26.20 ±5.13	26.67 ±5.08	26.63 ±4.42	0.77	26.01 ±4.53	26.87 ±4.99	26.56 ±5.10	0.48
Physical activity (MET-h/wk)	407.73 ±519.13	355.29 ±446.40	498.28 ±671.78	366.19 ±377.67	0.12	319.75 ±448.36	465.55 ±651.26	441.27 ±422.15	0.13	515.31 ±710.10	350.29 ±345.30	363.23 ±435.21	0.06
Headache duration (Hour)	10.03 ±10.78	13.82 ±14.74	8.38 ±7.06	7.87 ±7.86	<0.001	13.46 ±14.23	9.99 ±10.17	6.50 ±4.04	<0.001	7.25 ±7.98	10.88 ±11.31	11.92 ±12.13	0.01
Qualitative variables													
Marital status (n (%))					0.61				0.97				0.63
Single	74 (27.8)	20 (35.7)	27 (29.7)	27 (34.6)		25 (33.7)	24 (32.6)	25 (33.7)		29 (39.1)	23 (31)	22 (29.9)	
Married	192 (72.2)	69 (36)	64 (33.3)	59 (30.7)		66 (34.3)	64 (33.3)	62 (32.4)		57 (29.6)	73 (38)	62 (32.4)	
Education status (n (%))					0.16				0.60				0.65
≤Diploma	104 (39.1)	36 (34.7)	37 (35.5)	31 (29.8)		31 (29.8)	32 (30.7)	41 (39.4)		32 (30.7)	37 (35.5)	35 (33.8)	
>Diploma	162 (60.9)	53 (32.8)	54 (33.3)	55 (33.9)		60 (37.6)	56 (32.2)	46 (30.2)		54 (33.3)	59 (36.4)	49 (30.3)	
Current smoker (n (%))					0.35				0.11				0.06
Yes	13 (4.9)	2 (15.5)	6 (46.1)	5 (38.4)		1 (1.1)	6 (6.8)	6 (6.9)		8 (9.3)	3 (3.1)	2 (2.4)	
No	253 (95.1)	87 (34.5)	85 (33.5)	81 (32)		90 (98.9)	82 (93.2)	81 (93.1)		78 (90.7)	93 (96.9)	82 (97.6)	

PDI, overall plant-based diet index; hPDI, healthful plant-based diet index; uPDI, unhealthful plant-based diet index.
Values are mean± SD for quantitative variables and percentage for qualitative variables.
Using one-way ANOVA for quantitative variables and Chi-square test for qualitative variables

Fatty Acid (MUFA), cholesterol, vitamin B12, calcium, sodium, refined grains, fish/seafood, meats, animal fats, and miscellaneous animal-based foods compared with those in the bottom tertile. Moreover, participants in the top tertile of hPDI had higher intake of fiber, PUFA, vitamin A, C, B6, folic acid ,magnesium, potassium, whole grains, vegetables, fruit, legumes, nuts, vegetable oils, and tea/coffee, while they had lower intake of energy, protein, carbohydrate, fat, SFA, cholesterol, vitamin B12, sodium, sugar-sweetened beverages, refined grains, potatoes, sweets/desserts, dairy, fruits juice, animal fats, and miscellaneous animal-based foods. Moreover, the consumption of MUFA, thiamine, eggs, and meats across tertiles of hPDI, and energy protein, carbohydrate, thiamine, calcium, sugar- sweetened beverages, sweets/desserts,

Table 2. Dietary intakes of study participants across the tertiles (T) of PDI, hPDI, and uPDI

	PDI			p-value	hPDI			p value	uPDI			p value
	T1 ≤94 (N=89)	T2 95-104 (N=91)	T3 ≥105 (N=86)		T1 ≤89 (N=91)	T2 90-111 (N=88)	T3 ≥112 (N=87)		T1 ≤96 (N=86)	T2 97-106 (N=96)	T3 ≥107 (N=84)	
Nutrients												
Energy (*kcal/d*)	2310.76 ±512.57	2199.92 ±596.75	2181.37 ±427.57	0.20	2601.13 ±356.64	2129.78 ±497.26	1946.26 ±459.96	<0.001	2289.43 ±499.92	2135.93 ±546.76	2279.86 ±497.84	0.08
Protein (*g*/day)	80.93 ±12.47	77.13 ±15.70	79.88 ±19.11	0.25	83.03 ±11.80	77.24 ±15.76	77.46 ±19.15	0.02	84.08 ±18.68	76.32 ±14.79	77.80 ±13.06	0.003
Carbohydrate (*g*/day)	285.98 ±65.09	286.13 ±73.18	306.17 ±64.97	0.08	319.83 ±52.67	286.08 ±73.47	270.59 ±68.58	<0.001	305.21 ±72.73	279.70 ±69.64	294.31 ±59.80	0.04
Dietary fiber (*g*/day)	36.14 ±13.43	39.21 ±14.38	41.89 ±15.98	0.03	32.32 ±12.48	38.80 ±13.97	46.34 ±14.42	<0.001	42.74 ±16.85	38.21 ±12.60	36.21 ±14.10	0.01
Fat (*g*/day)	98.95 ±33.27	89.49 ±33.94	78.76 ±20.13	<0.001	115.05 ±25.12	81.12 ±25.47	70.30 ±22.24	<0.001	89.50 ±28.13	85.51 ±31.79	93.07 ±32.48	0.26
SFA (*g*/day)	31.77 ±12.38	28.60 ±13.60	23.11 ±9.12	<0.001	40.66 ±10.23	23.54 ±7.59	18.91 ±5.52	<0.001	26.37 ±10.65	27.17 ±12.26	33.35 ±13.22	0.005
MUFA (*g*/day)	32.95 ±12.87	29.38 ±12.79	25.38 ±8.65	<0.001	24.24 ±9.00	26.32 ±11.14	22.91 ±9.92	0.08	30.22 ±11.55	27.17 ±12.26	30.74 ±11.95	0.09
PUFA (*g*/day)	14.62 ±5.58	16.92 ±8.77	18.72 ±9.22	0.004	14.50 ±7.34	16.77 ±8.32	20.88 ±7.13	<0.001	17.64 ±8.08	15.22 ±8.08	17.67 ±8.26	0.06
Cholesterol (*mg*/day)	266.62 ±93.87	246.09 ±100.54	225.03 ±81.58	0.01	320.66 ±84.99	224.28 ±69.37	190.33 ±71.49	<0.001	252.88 ±93.18	246.04 ±99.10	239.37 ±88.35	0.64
Vitamin A (RAE/day)	635.88 ±179.60	716.02 ±253.93	789.45 ±426.53	0.004	607.78 ±125.45	603.58 ±256.05	933.58 ±369.22	<0.001	834.72 ±408.08	718.72 ±256.02	581.68 ±156.40	<0.001
Vitamin C (*mg*/day)	101.16 ±47.39	130.31 ±56.83	185.28 ±119.72	<0.001	87.75 ±27.85	133.53 ±89.93	196.10 ±91.91	<0.001	182.37 ±118.46	134.82 ±64.19	97.26 ±39.73	<0.001
Thiamine (*mg*/day)	1.71 ±0.49	1.69 ±0.57	1.68 ±0.49	0.91	1.78 ±0.44	1.69 ±0.60	1.62 ±0.50	0.12	1.75 ±0.55	1.58 ±0.51	1.78 ±0.47	0.08
Vitamin B6 (*mg*/day)	1.79±0.33	1.86 ±0.38	2.02 ±0.61	0.003	1.73 ±0.32	1.82 ±0.39	2.13 ±0.54	<0.001	2.10 ±0.58	1.86 ±0.39	1.72 ±0.30	<0.001
Folic acid (*µg*/day)	501.50 ±114.96	526.64 ±112.90	558.94 ±153.67	0.01	490.40 ±10.85	531.95 ±136.58	565.38 ±131.28	<0.001	570.44 ±138.92	510.30 ±132.48	506.90 ±105.99	0.001
Vitamin B12 (*µg*/day)	4.03 ±1.37	3.48 ±1.43	3.19 ±1.29	<0.001	4.56 ±1.26	3.50 ±1.24	2.61 ±0.96	<0.001	3.60 ±1.37	3.38 ±1.44	3.75 ±1.39	0.21
Calcium (*mg*/day)	1303.2 ±551.81	1312.77 ±473.13	1185.33 ±379.33	0.13	1566.55 ±596.21	1240.25 ±322.72	1007.27 ±257.20	<0.001	1413.45 ±576.40	1261.86 ±450.86	1123.79 ±319.38	<0.001
Magnesium (*mg*/day)	373.08 ±87.27	395.93 ±107.26	430.14 ±142.58	0.004	361.21 ±79.41	385.24 ±96.45	453.77 ±144.46	<0.001	449.96 ±152.12	381.41 ±84.24	368.31 ±85.43	<0.001
Potassium (*mg*/day)	3625.60 ±950.03	4031.96 ±1138.02	4505.45 ±1804.10	<0.001	3272.54 ±620.11	3908.96 ±985.16	5003.06 ±1710.91	<0.001	4702.45 ±1740.3	4008.2 ±1161.34	3426.88 ±788.36	<0.001
Sodium (*mg*/day)	4007.84 ±757.15	3659.81 ±815.30	3564.62 ±815.30	<0.001	3938.92 ±950.12	3739.62 ±735.20	3549.08 ±605.07	0.004	3713.84 ±684.0	3677.18 ±829.46	3855.94 ±848.96	0.29
Foods												
Whole grains (*g*/day)	34.09 ±44.51	55.01 ±51.88	79.35 ±93.21	<0.001	37.48 ±41.82	44.33 ±56.36	86.78 ±89.28	<0.001	85.58 ±94.76	40.20 ±39.34	43.36 ±51.69	<0.001
Vegetables (*g*/day)	196.66 ±96.88	252.61 ±118.02	305.67 ±140.45	<0.001	153.08 ±62.20	240.83 ±109.67	363.86 ±101.86	<0.001	304.56 ±142.21	253.76 ±118.68	193.16 ±91.25	<0.001
Fruit (*g*/day)	216.02 ±108.27	285.33 ±129.67	459.18 ±274.60	<0.001	245.04 ±107.72	333.82 ±257.65	379.38 ±216.66	<0.001	432.39 ±273.05	302.04 ±152.52	220.22 ±119.75	<0.001
Nuts (*g*/day)	3.41 ±2.70	3.35 ±2.36	4.34 ±3.94	0.008	3.18 ±3.07	3.79 ±3.36	4.36 ±2.79	<0.001	4.77 ±3.75	3.26 ±2.54	3.38 ±2.74	0.002
Legumes (*g*/day)	39.12 ±36.52	49.88 ±37.83	80.09 ±45.70	<0.001	39.79 ±32.02	59.35 ±43.69	69.70 ±48.56	<0.001	71.25 ±48.64	55.16 ±43.72	41.50 ±31.42	<0.001
Vegetable oil (*g*/day)	6.86 ±5.07	8.11 ±4.66	12.63 ±8.42	<0.001	7.64 ±3.51	9.87 ±8.07	14.00 ±7.44	<0.001	12.69 ±8.27	7.61 ±5.00	7.02 ±4.67	<0.001
Tea and coffee (*g*/day)	510.88 ±369.04	696.02 ±333.32	700.56 ±350.16	<0.001	555.05 ±266.70	751.16 ±376.53	705.08 ±377.16	<0.001	731.19 ±371.39	693.10 ±314.45	577.80 ±358.27	0.01
Sugar-sweetened beverages (*g*/day)	33.98 ±57.97	42.97 ±66.86	46.92 ±61.87	0.17	62.00 ±77.20	24.99 ±43.71	15.03 ±17.31	<0.001	29.90 ±47.86	47.23 ±73.84	46.47 ±60.45	0.11
Refined grains (*g*/day)	369.70 ±172.43	314.96 ±155.45	262.90 ±130.31	<0.001	401.66 ±128.29	319.05 ±172.61	224.67 ±121.33	<0.001	270.79 ±138.58	299.58 ±157.74	382.45 ±161.50	<0.001
Potato (*g*/day)	18.95 ±17.46	21.95 ±22.44	27.20 ±25.95	0.04	34.56 ±24.54	22.80 ±22.85	9.95 ±7.98	<0.001	18.11 ±18.77	22.92 ±21.71	29.76 ±26.06	0.002
Sweet dessert (*g*/day)	55.30 ±69.65	64.49 ±80.74	72.06 ±86.52	0.12	128.03 ±89.58	41.33 ±56.64	20.11 ±31.10	<0.001	53.03 ±66.76	63.82 ±86.93	75.60 ±81.53	0.18
Fruits juice (*g*/day)	5.40 ±13.29	13.94 ±20.18	38.81 ±46.69	<0.001	24.57 ±38.32	26.39 ±36.06	6.89 ±18.17	<0.001	9.64 ±19.08	16.89 ±22.12	30.87 ±47.70	<0.001
Dairy (*g*/day)	291.05 ±103.57	274.76 ±106.07	269.30 ±97.78	0.34	313.74 ±93.02	286.29 ±114.47	233.60 ±82.07	<0.001	297.50 ±103.34	266.47 ±82.77	272.62 ±119.51	0.10
Fish and seafood (*g*/day)	14.27 ±10.02	12.76 ±13.77	9.48 ±8.74	0.01	14.87 ±8.67	11.11 ±10.09	10.33 ±13.73	0.01	15.58 ±13.54	10.06 ±9.29	11.02 ±9.56	0.002

Eggs (g/day)	19.19 ±9.20	18.66 ±10.90	19.07 ±8.71	0.93	20.07 ±10.05	19.72 ±8.77	17.05 ±9.86	0.07	21.85 ±9.95	18.75 ±9.57	16.26 ±8.61	0.001
Meats (g/day)	68.19 ±31.48	61.60 ±28.23	53.32 ±27.65	0.003	65.77 ±29.29	61.40 ±31.35	55.51 ±27.77	0.06	61.85 ±29.72	59.26 ±25.78	62.03 ±33.85	0.78
Animal fat (g/day)	38.15 ±28.15	30.29 ±23.45	16.70 ±15.37	<0.001	46.41 ±23.73	21.41 ±21.07	17.01 ±17.21	<0.001	25.13 ±22.94	26.66 ±23.24	34.14 ±26.86	0.03
Miscellaneous animal-based foods (g/day)	20.04 ±18.87	15.30 ±19.85	13.34 ±15.89	0.04	32.63 ±16.93	10.86 ±14.71	4.57 ±8.94	<0.001	13.88 ±17.09	16.81 ±19.18	18.40 ±19.13	0.24

PDI, overall plant-based diet index; hPDI, healthful plant-based diet index; uPDI, unhealthful plant-based diet index; SFA: saturated fatty acid; PUFA: polyunsaturated fatty acid; MUFA; monounsaturated fatty acid.
Except total energy, all values are adjusted for energy intake.
Values are expressed as mean ± SD.
Using ANCOVA for dietary intake variables

dairy, and eggs across tertiles of PDI did not show any significant differences. In addition, individuals in the top uPDI tertile in comparison with those in the bottom tertile had lower intake of protein, carbohydrate, fiber, MUFA, cholesterol, folic acid, vitamin A, B6, folic acid, C, calcium, magnesium, potassium, whole grains, vegetables, fruit, nuts, legumes, vegetable oils, tea/coffee, eggs, fish/seafood, while higher intake of SFA, refined grains, potatoes, fruit juice, and animal fats was observed.

Plant-based diet indices and migraine headache

The association between severity, disability, and duration of migraine headache across tertiles of PDI, hPDI, and uPDI tertiles in crude model and adjusted model is shown in table 3. In the crude model of multinomial logistic regression, the greatest adherence to the PDI did not show a significant relation with severe pain based on VAS score (OR=0.71; 95% CI: 0.45, 1.10; p=0.12) and severe disability based on MIDAS score (OR=0.71; 95% CI: 0.44, 1.14; p=0.15). Even after adjustment for potential confounding factors, no association was observed between PDI and high VAS score (OR=0.76; 95% CI: 0.46, 1.26; p=0.29), and high MIDAS score (OR=0.75; 95% CI: 0.43, 1.30; p=0.30).

A significant inverse association was observed between hPDI and 65% lower rate of severe pain headaches (OR=0.35; 95% CI: 0.21, 0.57; p<0.001) and 43% lower rate of severe disability (OR=0.57; 95% CI: 0.35, 0.93; p=0.02) in crude model. After adjustment for the potential confounding factors, participants in the top tertile of hPDI were 60% and 50% less likely to have severe pain (OR=0.40; 95% CI: 0.21, 0.74; p=0.003) and severe disabling headaches (OR=0.50; 95% CI: 0.26, 0.95; p=0.03), respectively, compared with those in the bottom tertile. Subjects in the top tertile of uPDI

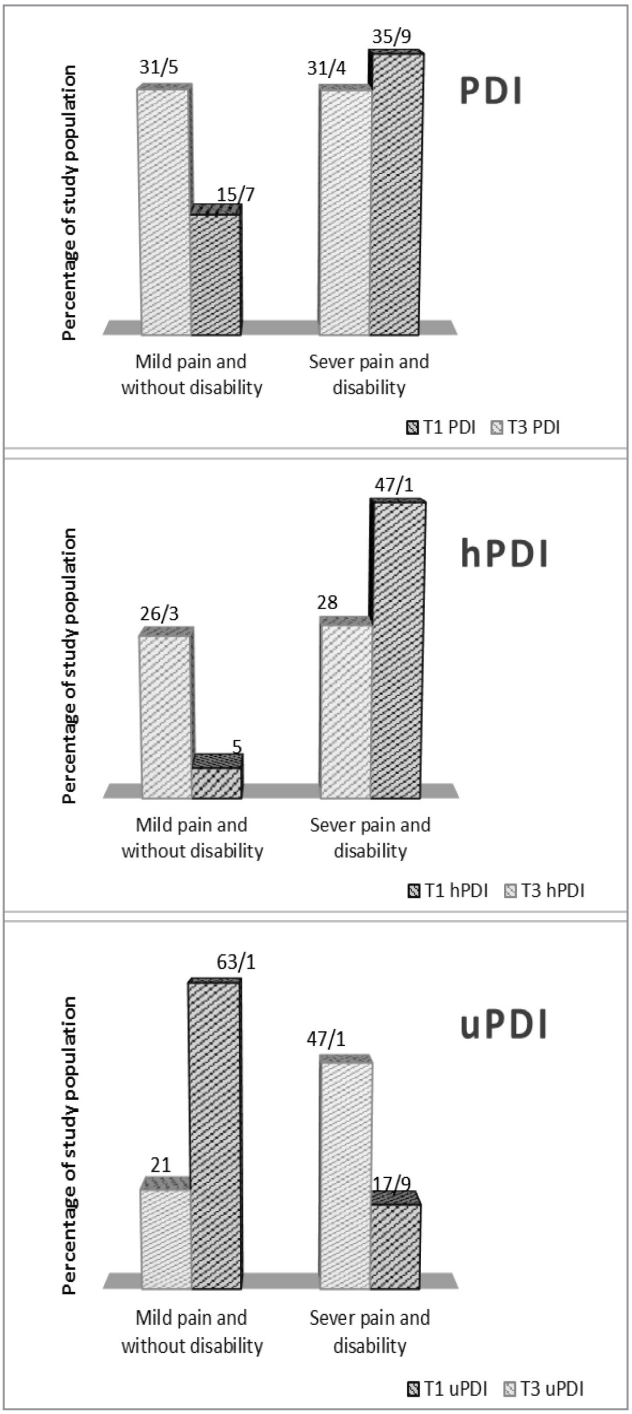

Figure 1. Percentage of T1 vs. T3 of PDI, hPDI, and uPDI among patients with severe or mild pain and severe or without disability (Based on VAS and MIDAS scores).

Table 3. Crude and multivariable adjusted odds ratios for pain, disability, and duration of migraine headache across PDI, hPDI, and uPDI scores

PDI						
	Crude models		**p-value**	**Adjusted models**		**p value**
	OR	**(0.95% CI)**		**OR**	**(0.95% CI)**	
Mild pain∞	-	-	-	-	-	-
Moderate pain	0.74	(0.47, 1.16)	0.19	0.79	(0.49, 1.28)	0.34
Severe pain	0.71	(0.45, 1.10)	0.12	0.76	(0.46, 1.26)	0.29
MIDAS						
Without disability∞	-	-	-	-	-	-
Mild disability	0.79	(0.47, 1.32)	0.38	0.83	(0.48, 1.43)	0.51
Moderate disability	0.82	(0.47, 1.44)	0.50	0.87	(0.48, 1.60)	0.67
Severe disability	0.71	(0.44, 1.14)	0.15	0.75	(0.43, 1.30)	0.30
Headache duration of each attack	*-0.12	(-3.16, 0.02)	0.08	*-0.10	(-2.86, 0.23)	0.21
hPDI						
	Crude models		**p-value**	**Adjusted models**		**p value**
	OR	**(0.95% CI)**		**OR**	**(0.95% CI)**	
VAS						
Mild pain∞	-	-	-	-	-	-
Moderate pain	0.43	(0.26, 0.70)	0.001	0.51	(0.28, 0.92)	0.02
Severe pain	0.35	(0.21, 0.57)	<0.001	0.40	(0.21, 0.74)	0.003
MIDAS						
Without disability∞	-	-	-	-	-	-
Mild disability	0.62	(0.37, 1.04)	0.07	0.60	(0.32, 1.11)	0.10
Moderate disability	0.68	(0.39, 1.20)	0.19	0.61	(0.30, 1.22)	0.16
Severe disability	0.57	(0.35, 0.93)	0.02	0.50	(0.26, 0.95)	0.03
Headache duration of each attack	*-0.26	(-5.01, -1.94)	<0.001	*-0.21	(-4.69, -1.08)	0.002
uPDI						
	Crude models		**p-value**	**Adjusted models**		**p value**
	OR	**(0.95% CI)**		**OR**	**(0.95% CI)**	
VAS						
Mild pain∞	-	-	-	-	-	-
Moderate pain	1.13	(0.70, 1.80)	0.60	1.23	(0.73, 2.05)	0.43
Severe pain	2.50	(1.56, 4.02)	0.001	3.00	(1.72, 5.23)	<0.001
MIDAS						
Without disability∞	-	-	-	-	-	-
Mild disability	1.35	(0.79, 2.33)	0.26	1.39	(0.78, 2.45)	0.25
Moderate disability	1.70	(0.95, 3.06)	0.07	1.86	(0.98, 3.57)	0.05
Severe disability	2.21	(1.32, 3.68)	0.002	2.50	(1.39, 4.51)	0.001
Headache duration of each attack	*0.11	(-0.06, 2.94)	0.12	*0.08	(-0.26, 2.74)	0.23

PDI, overall plant-based diet index; hPDI, healthful plant-based diet index; uPDI, unhealthful plant-based diet index; MIDAS, Migraine Disability Assessment questionnaire; VAS, Visual Analog Scale.
* The β coefficient has been shown.
a Adjusted for confounders.
∞ Considered as reference group

compared with those in the bottom tertile were more likely to have a higher odds of severe pain in crude (OR=2.50; 95% CI: 1.56, 4.02; p=0.001) and adjusted models (OR=3.00; 95% CI:1.72, 5.23; p<0.001) or severe disability in crude (OR=2.21; 95% CI: 1.32, 3.68; p=0.002) and adjusted models (OR=2.50; 95% CI: 1.39, 4.51; p=0.001).

Linear Regression Model (LRM) indicated a statistically significant inverse association between mean duration of each headache attack in the last

three months and hPDI score in crude (β=-0.26, 95% CI=-5.01, -1.94, p<0.001) and adjusted models (β=-0.21, 95% CI=-4.69, -1.08, p=0.002). However, PDI score in crude (β=-0.12, 95% CI=-3.16, 0.02, p=0.08) and adjusted models (β=-0.10, 95% CI=-2.86, 0.23, p=0.21), as well as uPDI score in crude (β= 0.11, 95% CI=-0.06, 2.94, p=0.12) and adjusted models (β=0.08, 95% CI=-0.26, 2.74, p=0.23) showed no statistically significant correlation with headache duration.

Discussion

This is the first study that addresses the association between adherence to plant-based diets and headache severity and duration among migraine patients. Our main analyses showed that there was no significant association between PDI scores and risk of migraine headaches. However, greater hPDI scores were significantly associated with reduced headache intensity and duration. In contrast, a higher score of uPDI was directly associated with more headaches.

Formerly, foods were classified into two main groups of animal and plant sources. Plant sources were believed to be the optimum choice in order to have a healthy life (24). However, later on, it was discovered that not all plant foods impose such effects. For instance, high consumption of sugar-sweetened beverages, potatoes, and refined grains could increase the risk of diabetes and heart diseases (14,25). Therefore, to have a better insight into this matter, the association between migraine and PDI, hPDI, and uPDI was examined separately.

There are possible mechanisms through which the hypothesis of the effect of plant-based diet on migraine could be justified. Migraine is a neurovascular disorder, induced through a set of actions starting within the brain and then spreading to the blood vessels (26). Sudden changes in blood flow to the brain may contribute to the pain (27). Calcitonin Gene-Related Peptide (CGRP) is a member of the calcitonin family of peptides, produced in neurons. CGRP acts as a strong vasodilator and could cause neurogenic inflammation (28). The evidence suggesting the role of CGRP in migraine is numerous. Goadsby *et al* found that serum level of CGRP was elevated following a migraine attack (29). Moreover, a causative role of CGRP was also discovered when it induced migraine headaches after it was intravenously infused in patients (30). CGRP antagonists were shown to reduce the average number of migraine days in migraine sufferers (31). Several studies indicated that food intake could also be capable of altering CGRP levels (32,33). Glucosinolate and sulforaphane which are the natural components of some vegetables such as cabbage, broccoli, beets, parsley, spinach, and carrots categorized as healthy plants were also found to prevent migraine with an antagonistic ability against CGRP, even better than administered drugs in some cases (34).

Moreover, it has been proposed that inflammation, with sensitization of nerve endings in meninges, could play a significant role in migraine pain. According to recent studies, high sensitivity c-reactive protein (hsCRP) was elevated in adults with migraine (35,36); these findings advocate treatments which exert anti-inflammatory effects. Healthy plant foods are rich sources of fiber and antioxidants (37). High-fiber diets reduce inflammation via slowing glucose absorption, altering gut microflora, and suppressing the production of inflammatory cytokines (38). In addition, nutritional antioxidants protect the body cells from the free radicals and act in favor of anti-inflammatory balance (39).

Healthy plant foods contain a high level of magnesium, a nutrient that could have a key role in the management of migraine. Several studies have shown that migraineurs have low brain magnesium during migraine attacks and may also have a magnesium deficiency (40,41). Two clinical trial studies have revealed that oral magnesium supplementation could have a major role in attenuating headaches (42,43). These beneficial effects of magnesium could be due to its impact on the regulation of blood pressure (44) or its anti-inflammatory properties (45) as, findings from a meta-analysis of seven cross-sectional studies showed an inverse association between serum hs-CRP concentration and magnesium intake (46). Moreover, low serum levels of magnesium and riboflavin (which is also found abundantly in plant foods) could attribute to mitochondrial dysfunction, a complication which may lead to migraine headaches through causing changes in heart rate and blood pressure (47,48).

According to our findings, the high consumption of

unhealthy plant foods is positively related to migraine headaches. Greater adherence to uPDI is equivalent to diets with higher glycemic load and index and lower levels of dietary fiber, micronutrients, and antioxidants (49). Studies revealed that hyperglycemia may be associated with higher levels of inflammation markers (50,51). Moreover, according to several studies, a higher glycemic diet, due to its adverse impact on blood vessels may lead to hypertension (52,53).

There are certain limitations in our study which are worth considering. The study population was relatively small. Significant sex differences in migraine have been proposed in previous studies (54), while the participants of this study were limited to women. If men were also presented, significant findings could have been obtained. In addition, questionnaire responses were based on participants' memory and their feeling of pain. Our evidence is associational and does not prove causality. Firm conclusions cannot be drawn from one single study such as ours. Instead, it is better to assess a possible association by using results from multiple epidemiological studies, ideally in different populations and/or countries.

Conclusion

In conclusion, our findings showed that higher adherence to the plant-based diet, particularly healthy plants, may be associated with lower headache severity, disability and duration. In addition, unhealthy plants may be related with more risk of migraine headaches.

Acknowledgements

The authors thank the participants and the staff at Neurology clinics of Sina and Khatam-al- Anbya Hospitals. M. A., A. S., F. K., L. S., M. T., and K. M. contributed in data collection and interpretation, design, conception, manuscript drafting, statistical analyses, and approval of the final version of the manuscript and accepted all aspects of the work.

The present study protocol was confirmed (Ethics code: IR.TUMS.REC.1394.2141) by the Research Committee of the School of Nutritional Sciences and Dietetics of Tehran University of Medical Sciences (TUMS). This study was extracted from a dissertation that was confirmed by Tehran University of Medical Sciences (Grants ID: 95-01- 103-31348). The authors report no conflict of interest.

References

1. Dodick DW, Silberstein SD, Bigal ME Paul P Yeung PP, Goadsby PJ, Blankenbiller T, et al. Effect of fremanezumab compared with placebo for prevention of episodic migraine: a randomized clinical trial. JAMA 2018;319(19):1999-2008.

2. Lanteri-Minet M. Economic burden and costs of chronic migraine. Curr Pain Headache Rep 2014;18(1):385.

3. Steiner TJ, Stovner LJ, Vos T et al. Migraine is first cause of disability in under 50s: will health politicians now take notice? J Headache Pain 2018;19(1):17.

4. Leonardi M, Raggi A. Burden of migraine: international perspectives. Neurol Sci 2013;34 (Suppl 1):S117-8.

5. Stovner L, Hagen K, Jensen R, Katsarava Z, Lipton R, Scher A, et al. The global burden of headache: a documentation of headache prevalence and disability worldwide. Cephalalgia 2007;27(3):193-210.

6. Pardutz A, Schoenen J. NSAIDs in the acute treatment of migraine: A review of clinical and experimental data. Pharmaceuticals (Basel) 2010;3(6):1966-87.

7. Harirforoosh S, Asghar W, Jamali F. Adverse effects of nonsteroidal antiinflammatory drugs: an update of gastrointestinal, cardiovascular and renal complications. J Pharm Pharm Sci 2013;16(5):821-47.

8. Evans EW, Lipton RB, Peterlin BL, Raynor HA, Thomas JG, O'Leary KC, et al. Dietary intake patterns and diet quality in a nationally representative sample of women with and without severe headache or migraine. Headache

2015;55(4):550-61.

9. Amer M, Woodward M, Appel LJ. Effects of dietary sodium and the DASH diet on the occurrence of headaches: results from randomised multicentre DASH-Sodium clinical trial. BMJ Open 2014;4(12):e006671.

10. McMacken M, Shah S. A plant-based diet for the prevention and treatment of type 2 diabetes. J Geriatr Cardiol 2017;14(5):342-54.

11. Satija A, Bhupathiraju SN, Spiegelman D, Chiuve SE, Manson JE, Willett W, et al. Healthful and unhealthful plant-based diets and the risk of coronary heart disease in U.S. adults. J Am Coll Cardiol 2017;70(4):411-22.

12. Lanou AJ, Svenson B. Reduced cancer risk in vegetarians: an analysis of recent reports. Cancer Manag Res 2010;3:1-8.

13. Sun-Edelstein C, Mauskop A. Foods and supplements in the management of migraine headaches. Clin J Pain 2009;25(5):446-52.

14. Sadeghi O, Hassanzadeh-Keshteli A, Afshar H Esmaillzadeh A, Adibi P. The association of whole and refined grains consumption with psychological disorders among Iranian adults. Eur J Nutr 2019;58(1):211-25.

15. Esmaillzadeh A, Azadbakht L. Major dietary patterns in relation to general obesity and central adiposity among Iranian women. J Nutr 2008;138(2):358-63.

16. Mirmiran P, Hosseini-Esfahani F, Jessri M, Mahan LK, Shiva N, Azizi F.et al. Does dietary intake by Tehranian adults align with the 2005 dietary guidelines for Americans? Observations from the Tehran lipid and glucose study. J Health Popul Nutr 2011;29(1):39-52.

17. Satija A, Bhupathiraju SN, Rimm EB, Spiegelman D, Chiuve SE, Borgi L, et al. Plant-based dietary patterns and incidence of type 2 diabetes in US men and women: results from three prospective cohort studies. PLoS Med 2016;13(6):e1002039.

18. Levin M. The international classification of headache disorders, (ICHD III)–changes and challenges. Headache: The Journal of Head and Face Pain 2013;53:1383-95.

19. Elrington G. Migraine: diagnosis and management. J Neurol Neurosurg Psychiatry 2002;72 Suppl 2(Suppl 2):ii10-ii15.

20. Ghorbani A, Chitsaz A. Comparison of validity and reliability of the Migraine disability assessment (MIDAS) versus headache impact test (HIT) in an Iranian population. Iran J Neurol 2011;10(3-4):39-42.

21. Stewart WF, Lipton RB, Dowson AJ, Sawyer J. Development and testing of the Migraine Disability Assessment (MIDAS) Questionnaire to assess headache-related disability. Neurology 2001;56(Suppl 6):S20-8.

22. Price DD, McGrath PA, Rafii A, Buckingham BV. The validation of visual analogue scales as ratio scale measures for chronic and experimental pain. Pain 1983;17(1):45-56.

23. Wanner M, Probst-Hensch N, Kriemler S, Meier F, Autenrieth C, Martin BW. (2016) Validation of the long international physical activity questionnaire: Influence of age and language region. Preventive Medicine Reports 2016;3:250-6.

24. Turner-McGrievy G, Mandes T, Crimarco A. A plant-based diet for overweight and obesity prevention and treatment. J Geriatr Cardiol 2017;14(5):369-74.

25. Gangwisch JE, Hale L, Garcia L, Malaspina D , Opler MG, Payne ME, et al. High glycemic index diet as a risk factor for depression: analyses from the Women's Health Initiative. Am J Clin Nutr 2015;102(2):454-63.

26. Buse DC, Greisman JD, Baigi K, Lipton RB. Migraine progression: A systematic review. Headache 2019;59(3):306-38.

27. Bahra A, Matharu M, Buchel C, Frackowiak RS, Goadsby PJ. Brainstem activation specific to migraine headache. Lancet 2001;357(9261):1016-7.

28. Durham PL. CGRP-receptor antagonists--a fresh approach to migraine therapy? N Engl J Med 2004;350(11):1073-5.

29. Goadsby PJ, Edvinsson L. The trigeminovascular system and migraine: studies characterizing cerebrovascular and neuropeptide changes seen in humans and cats. Ann Neurol 1993;33(1):48-56.

30. Lassen LH, Haderslev PA, Jacobsen VB, Iversen HK, Sperling B, Olesen J. CGRP may play a causative role in migraine. Cephalalgia 2002;22(1):54-61.

31. Urits I, Jones MR, Gress K Charipova K, Fiocchi J, Kaye AD, et al. CGRP antagonists for the treatment of chronic migraines: a comprehensive review. Curr Pain Headache Rep 2019;23(5):29.

32. Katz DL, Doughty K, Ali A. Cocoa and chocolate in human health and disease. Antioxid Redox Signal 2011;15(10):2779-811.

33. Slavin M, Bourguignon J, Jackson K, Orciga MA. Impact of food components on in vitro calcitonin gene-related peptide secretion-a potential mechanism for dietary influence on migraine. Nutrients 2016;8(7):406.

34. Jain MM, Kumari N, Rai G. A novel formulation of veggies with potent anti–migraine activity. Int J Comput Biol Drug Des 2015;8(1):54-61.

35. Lippi G, Mattiuzzi C, Cervellin G. C-reactive protein and migraine. Facts or speculations? Clin Chem Lab Med 2014;52(9):1265-72.

36. Tietjen GE, Herial NA, White L, Utley C, Kosmyna JM, Khuder SA. Migraine and biomarkers of endothelial activation in young women. Stroke 2009;40(9):2977-82.

37. Carlsen MH, Halvorsen BL, Holte K, Bøhn SK, Dragland S, Sampson L, et al. The total antioxidant content of more than 3100 foods, beverages, spices, herbs and supplements used worldwide. Nutr J 2010 22;9:3.

38. Estruch R, Martinez-Gonzalez MA, Corella D, Basora-Gallisá J, Ruiz-Gutiérrez V, Covas MI, et al. Effects of dietary fibre intake on risk factors for cardiovascular disease in subjects at high risk. J Epidemiol Community Health 2009;63(7):582-8.

39. Grimble RF. Nutritional antioxidants and the modulation of inflammation: theory and practice. New Horiz 1994;2(2):175-85.

40. Mauskop A, Altura BM. Role of magnesium in the pathogenesis and treatment of migraines. Clin Neurosci 1998;5(1):24-7.

41. Ramadan NM, Halvorson H, Vande-Linde A, Levine SR, Helpern JA, Welch KM. Low brain magnesium in migraine. Headache 1989;29(7):416-9.

42. Facchinetti F, Sances G, Borella P, Genazzani AR, Nappi G. Magnesium prophylaxis of menstrual migraine: effects on intracellular magnesium. Headache 1991;31(5):298-301.

43. Peikert A, Wilimzig C, Kohne-Volland R. Prophylaxis of migraine with oral magnesium: results from a prospective, multi-center, placebo-controlled and double-blind randomized study. Cephalalgia 1996;16(4):257-63.

44. Rosanoff A. [Magnesium and hypertension]. Clinical Calcium 2005;15(2):255-60. [Japanese]

45. Nielsen FH. Effects of magnesium depletion on inflammation in chronic disease. Curr Opin Clin Nutr Metab Care 2014;17(6):525-30.

46. Dibaba DT, Xun P, He K. Dietary magnesium intake is inversely associated with serum C-reactive protein levels: meta-analysis and systematic review. Eur J Clin Nutr 2015;69(3):409.

47. Lodi R, Iotti S, Cortelli P, Pierangeli G, Cevoli S, Clementi V, et al. Deficient energy metabolism is associated with low free magnesium in the brains of patients with migraine and cluster headache. Brain Res Bull 2001;54(4):437-41.

48. Yorns WR Jr., Hardison HH. Mitochondrial dysfunction in migraine. Semin Pediatr Neurol 2013;20(3):188-93.

49. Satija A, Bhupathiraju SN, Spiegelman D, Chiuve SE, Manson JA, Willett W, et al. Healthful and unhealthful plant-based diets and the risk of coronary heart disease in U.S. adults. J Am Coll Cardiol 2017;70(4):411-22.

50. de Rekeneire N, Peila R, Ding J, Colbert LH, Visser M, Shorr RI, et al. Diabetes, hyperglycemia, and inflammation in older individuals: the health, aging and body composition study. Diabetes Care 2006;29(8):1902-8.

51. Tsalamandris S, Antonopoulos AS, Oikonomou E, Papamikroulis GA, Vogiatzi G, Papaioannou S, et al. The role of inflammation in diabetes: current concepts and future perspectives. Eur Cardiol 2019;14(1):50-9.

52. Evans CE, Greenwood DC, Threapleton DE, Gale DC, Cleghorn CL, Burley VJ, et al. Glycemic index, glycemic load, and blood pressure: a systematic review and meta-analysis of randomized controlled trials. Am J Clin Nutr 2017;105(5):1176-90.

53. Midha T, Krishna V, Shukla R, Katiyar R, Kaur S, Martolia DS, et al. Correlation between hypertension and hyperglycemia among young adults in India. World J Clin Cases 2015;3(2):171-9.

54. Peterlin BL, Gupta S, Ward TN Ward, MD, MacGregor A. Sex matters: evaluating sex and gender in migraine and headache research. Headache 2011;51(6):839-42.