

## ⇒ Research Article



# The Relationship Between Food Allergens and Migraine Among Patients With Migraine Referring to Shahid Mohammadi Neurology Clinic

Ahmadagha Negahi<sup>1</sup>, Ahmad Tamoradi<sup>2</sup>, Behnam Ahmadi<sup>2</sup>, Afsoon Piroozan<sup>3</sup>, Saeed Hosseini Tashnizi<sup>4</sup>

<sup>1</sup>Department of Neurology, Faculty of Medicine, Hormozgan University of Medical Sciences, Bandar Abbas, Iran

<sup>2</sup>Student Research Committee, Hormozgan University of Medical Sciences, Bandar Abbas, Iran

<sup>3</sup>School of Medicine, Hormozgan University of Medical Sciences, Bandar Abbas, Iran

<sup>4</sup>Infectious and Tropical Diseases Research Center, Hormozgan University of Medical Sciences, Bandar Abbas, Iran

## Abstract

**Background:** Although diet-induced migraines affect many people, the triggering foodstuffs are not fully identified yet. Detecting migraine-triggering foods and susceptible individuals assist in effective headache management. The aim of this study was to determine the relationship between eating allergens and developing or exacerbating migraine.

**Methods:** This was a descriptive-analytical cross-sectional study with 230 migraine patients referring to the neurology clinic of Shahid Mohammadi hospital in Bandar Abbas. They were selected through purposive sampling. After obtaining informed consent from the patients, the required data were collected and then underwent analysis.

**Results:** Overall, 52.4% and 47.6% of participants were females and males, respectively. Their mean age was  $40.57 \pm 14.04$ . Based on the results, 61.9% of participants were married, and 60.3% of them had a family history of migraine. The average number of headaches per month and the duration of each headache were 3.16-4.19 times and 3.76-4.41 hours, respectively. Based on the findings, sausages (55.6%), carbonated beverages (0.54%), peanuts (0.46%), beef (44.4%), and canned food, coffee, and eggs (41.3%) are the most common foodstuffs that cause or exacerbate migraines. On the other hand, chicken (15.9%), strawberry, rice, and wheat (17.5%) had the least impact on the onset and exacerbation of migraine headaches.

**Conclusion:** According to the results, identifying food allergens and eliminating them from patients' diets can be effective in the prognosis of migraine and individuals' quality of life.

**Keywords:** Headache, Migraines, Food allergens

## \*Correspondence to

Ahmadagha Negahi,  
Email: Drahmadnegahi@gmail.com



Received March 5, 2022, Accepted: May 14, 2022, Published Online: November 3, 2022

## Background

Headache has been a common problem among humans for ages, and everyone has developed a headache at least once in their lifetime. It is the most frequent complaint for which patients refer to neurology clinics (1). Headache, especially migraine, is considered a significant medical condition due to its chronic process and complications which influence individuals' quality of life. What we eat and our diet are the influencing factors of migraine. The headache which originates from the foodstuff is sudden in nature.

It has been reported that women are affected by migraine headaches at a rate nearly three times those of men (2). According to Mitchell et al, migraine headaches affect approximately 6%-7% of men and 20% of women (3). Food sensitivities have been linked to migraines for decades (4). Estimates suggest that 60% of the population may have food allergies or sensitivities and

not even know it (4).

According to previous studies, 50%-75% of patients with migraine are females. The earliest onset of the disease during the first decade of life is approximately 25%. About 55% and 90% of the cases develop the first onset below 20 and 40 years of age, respectively (5). Different studies report a 15% prevalence in the community, which is more common among females (5). In type I hypersensitivities, the immunoglobulin E (IgE) antibody is involved less than the other antibodies in the way that serum concentration levels defer between 0.1 and 0.3  $\mu\text{g}/\text{mL}$ .

Migraine is most frequently diagnosed with its stimulants. The brain becomes sensitive to different stimuli such as extreme light, noise, hunger, stress, physical exertion, air pressure variations, hormonal fluctuations during menstruation, shortage or excessive sleep, and alcohol consumption, along with other chemical stimuli (5). A descriptive cross-sectional study

investigated the correlation between migraine severity and IgE level in peripheral blood. The IgE level was recorded for all 212 participants and then scrutinized for the clinical signs of allergic rhinitis (AR). The prevalence of AR in migraine patients and the degree of allergic sensitivity were examined in this study. According to the findings, there was a 78.3% prevalence of AR among migraine patients. The IgE level in the peripheral blood was significantly higher among migraine patients with RA compared with people who did not have migraine. There was also a significant relationship between the intensity of AR (higher levels of IgE) and the severity of migraine attacks. However, no significant relationship was observed between AR intensity and other factors. Ultimately, the researchers concluded that inflammatory mediators play a key role in triggering migraine attacks. Hence, the effective treatment of AR is crucial in the treatment and prophylaxis of migraine headaches (6).

In another descriptive cross-sectional study, Rosario et al examined the relationship between allergic sensitivity with the prevalence of migraine and its accompanying disability. The serum IgE level was recorded for 100 male and female outpatients who were diagnosed with migraine. Moreover, migraine severity was evaluated with the Migraine Disability Assessment scale. It was detected that elevated levels of IgE were accompanied by more severe headaches which required longer treatments. Considering the findings, it was concluded that migraine is more prevalent among females and younger individuals (7).

Given the prevalence of migraine in Bandar Abbas and controversial reports regarding the relationship between migraine and serum IgE level, the present study sought to investigate this potential relationship through measuring the serum IgE level during the acute phase of migraine headache for patients who had been referred to the neurology clinic in Shahid Mohammadi Hospital in 2019. It is believed that the findings would have diagnostic, therapeutic, and prophylactic utility for the management of migraine headaches.

## Materials and Methods

The population of this cross-sectional descriptive-analytical study involved all patients who had been referred to the Neurology Clinic of Shahid Mohammadi Hospital in Bandar Abbas with the complaint of headache, for whom the diagnosis of migraine was confirmed. The minimum sample size was calculated as 230 individuals who were selected through purposive sampling. The inclusion criteria were having signed the informed consent form, being in the group age of 18-65 years, and having a confirmed diagnosis of migraine. On the other hand, the other types of headaches such as tension or cluster headaches, history of secondary headache disorders due to conditions (i.e., cerebral aneurysm or tumors), and

chronic medical disorders such as malignancies or renal failure in addition to pregnancy and its concomitant migraine were considered as the exclusion criteria.

The patients' demographic information such as age, gender, marital status, and other data such as a family history of headache, frequency, and duration of each headache in a given month were recorded in a questionnaire by the assistant physician. The quantitative data distribution was examined using the Kolmogorov-Smirnov test, and then the data were analyzed through statistical tests such as chi-square and Mann-Whitney.

## Results

The participants' demographic information indicated that out of 230 subjects, 121 (52.6%) were females and 109 (47.4%) of them were males. The mean age of the patients was  $40.59 \pm 13.80$ . Among them, 62.2% were married and 62.2% had a family history of migraine. The average number of headaches per month was  $4.20 \pm 3.13$ , and the duration of each was 3.52-4.24 hours.

Eating allergen foods (Table 1) cause or exacerbate migraine. According to the findings, sausages (55.7%), carbonated beverages (52.2%), peanut (45.2%), veal or beef (45.2%), and canned food (41.7%) were the most common foodstuff that could trigger or exacerbate migraine headaches, respectively. On the other hand, chicken, strawberry, rice, and wheat had the least potential in this regard.

The relationship between the potential of consumed food in the initiation or exacerbation of migraine headaches based on the gender of patients was examined through the cross-tab command by the chi-square test (Table 2). The results indicated that cantaloupe was the only fruit that had a significant relationship with migraine exacerbation ( $P < 0.05$ ). This was more evident among women.

According to the obtained results, the chi-square test revealed that none of the intended foodstuffs had a significant relationship with the migraine onset or deterioration in terms of family history ( $P > 0.05$ ) (Table 3).

Based on data analysis, the egg was the sole food that could significantly initiate or worsen migraine headaches ( $P < 0.05$ ) with a presumably higher degree among married patients compared with single ones (Table 4).

The data in Table 5 represent the relationship between the potential of eaten foodstuff on migraine initiation or exacerbation based on the participants' age. Due to the abnormal distribution of the participant's age, Mann-Whitney non-parametric test was applied to examine this relationship. According to the findings, none of the foodstuffs had a significant relationship with migraine initiation or exacerbation based on age ( $P > 0.05$ ).

Due to the abnormal distribution of patients' headache hours, Mann-Whitney non-parametric test was applied to examine the relationship between the consumed

**Table 1.** Frequency and Percentage of Consumed Migraine Aggravating Foods

Foodstuff	Impact on Migraine	
	No No. (%)	Yes No. (%)
Egg	136 (59.1)	94 (40.9)
Cereals		
Wheat	192 (83.5)	38 (16.5)
Soy	177 (77)	53 (23)
Barley	182 (82.2)	41 (17.8)
Rice	191 (83)	39 (17)
Dairy products		
Cow milk	147 (63.9)	83 (36.1)
Fruits		
Banana	177 (77)	53 (23)
Grapes	168 (73)	62 (27)
Kiwi	142 (60.9)	90 (39.1)
Strawberry	192 (83.5)	38 (16.5)
Cantaloupe	149 (64.8)	81 (35.2)
Watermelon	174 (75.7)	56 (24.3)
Meat		
Beef	126 (54.8)	104 (45.2)
Mutton	188 (81.7)	42 (18.3)
Chicken	197 (85.7)	33 (14.3)
Shrimp	157 (68.7)	73 (31.3)
Fish	181 (87.7)	49 (21.3)
Nuts		
Walnut	154 (67)	76 (33)
Hazelnut	160 (69.6)	70 (30.4)
Almond	157 (76.1)	55 (23.9)
Peanut	126 (54.8)	104 (45.2)
Carbonated beverages	110 (47.8)	120 (52.2)
Sausages	102 (44.3)	128 (55.7)
Canned food	134 (58.3)	96 (41.7)
Coffee	136 (59.1)	94 (40.9)
Traditional cheese	158 (68.7)	72 (31.3)
Industrial cheese	161 (70)	69 (30)
Cocoa	157 (68.3)	73 (31.7)

foodstuff on migraine onset and intensity. According to the findings, there was a significant relationship between the intake of traditional or industrial cheese and headache hours ( $P < 0.05$ ) (Table 6). In other words, patients who are non-allergic to cheese experience considerably less intense headaches.

Since the number of patients' headaches did not have a normal distribution, Mann-Whitney non-parametric test evaluated the relationship between the foodstuff and migraine intensity. It was found that eating shrimp had a significant relationship with migraine ( $P < 0.05$ ) (Table 7). It is apparent that patients who are non-allergic to shrimp

suffer from less severe migraine headaches.

## Results and Discussion

Migraine is a type of primary periodic headache which is accompanied by a combination of neurologic gastrointestinal and autonomic symptoms (1). Other symptoms include photophobia, nausea, vomiting, constipation or diarrhea, weight gain, ataxia, dizziness, hypertension, and fluid retention, followed by urination (2).

The findings of this study indicated that the most

**Table 2.** Evaluation of the Relationship Between the Triggering Potential of Foodstuffs on the Initiation and Exacerbation of Migraine Based on Patients' Gender

Foodstuff	Impact on Migraine		Chi-square Test	P Value
	Gender			
	Female	Male		
Egg	41	53	1.801	0.180
Cereals				
Wheat	14	24	1.371	0.242
Soy	23	30	1.210	0.271
Barley	13	28	2.156	0.142
Rice	22	17	0.025	0.874
Dairy products				
Cow milk	49	34	0.610	0.435
Fruits				
Banana	33	20	0.458	0.498
Grapes	37	25	0.387	0.534
Kiwi	55	35	0.965	0.326
Strawberry	28	10	2.212	0.137
Cantaloupe	59	22	5.610	0.018
Watermelon	33	23	0.458	0.498
Meat				
Beef	49	55	0.029	0.866
Mutton	25	17	0.211	0.646
Chicken	18	15	0.027	0.869
Shrimp	40	32	0.000	1.000
Fish	23	26	0.655	0.418
Nuts				
Walnut	38	38	0.000	1.000
Hazelnut	32	38	0.274	0.601
Almond	23	32	2.864	0.091
Peanut	51	52	0.363	0.547
Carbonated beverages	57	63	0.839	0.360
Sausages	67	61	0.029	0.866
Canned food	53	43	1.488	0.222
Coffee	51	42	1.488	0.222
Traditional cheese	43	29	0.682	0.409
Industrial cheese	37	32	0.001	0.979
Cocoa	59	25	1.145	0.285

**Table 3.** Evaluation of the Relationship Between the Triggering Potential of Foodstuffs on the Initiation and Exacerbation of Migraine Based on Family History

Foodstuff	Impact on Migraine		Chi-square Test	P Value
	Family History			
	Negative	Positive		
Egg	34	60	0.028	0.868
Cereals				
Wheat	12	26	0.061	0.804
Soy	24	29	0.401	0.526
Barley	19	22	0.659	0.417
Rice	12	27	0.061	0.804
Dairy products				
Cow milk	32	51	0.021	0.884
Fruits				
Banana	27	26	1.533	0.216
Grapes	45	17	1.026	0.311
Kiwi	57	33	0.002	0.967
Strawberry	23	15	0.185	0.667
Cantaloupe	54	27	0.156	0.693
Watermelon	39	17	0.332	0.565
Meat				
Beef	54	50	2.241	0.134
Mutton	20	22	0.659	0.417
Chicken	14	19	2.050	0.152
Shrimp	26	46	0.033	0.856
Fish	16	33	0.118	0.731
Nuts				
Walnut	34	42	0.829	0.363
Hazelnut	31	39	0.671	0.413
Almond	17	38	0.332	0.565
Peanut	36	68	0.069	0.793
Carbonated beverages	53	67	1.679	0.195
Sausages	58	70	1.197	0.274
Canned food	35	61	0.028	0.868
Coffee	40	54	0.775	0.379
Traditional cheese	34	38	1.303	0.254
Industrial cheese	34	35	1.906	0.167
Cocoa	25	48	0.033	0.856

common types of food that trigger migraine are sausages (55.6%), carbonated soft drinks (54%), peanut (46%), veal or beef (44%), canned food (41.3%), and coffee and eggs (41.3%). On the other hand, chicken, strawberry, rice, and wheat had the least effect on the initiation and exacerbation of migraine. Cantaloupe had a significant relationship solely with gender ( $P < 0.05$ ) so that it could trigger migraine mostly in women. According to the results, none of the foodstuffs had a significant relationship with family history ( $P > 0.05$ ). In a study conducted in Gilan, Iran, the prevalence of migraine was investigated

using an AR questionnaire among different age groups. It was concluded that the prevalence was 14.3% and 28.2% in the age groups of 6-7 and 12-13 years, respectively (8).

Based on our findings, a significant relationship was found between cheese consumption and patients' duration of headaches in terms of hours ( $P < 0.05$ ). In other words, patients who are allergic to traditional and industrial cheese suffer more intense migraine headaches.

The results of this study also revealed a significant relationship between eating shrimp and migraine onset or deterioration. It is apparent that patients who are non-

**Table 4.** Evaluation of the Relationship Between the Triggering Potential of Foodstuffs on the Initiation and Exacerbation of Migraine Based on Marital Status

Foodstuff	Impact on Migraine		Chi-square Test	P Value
	Marital Status			
	Single	Married		
Egg	18	76	6.680	0.010
Cereals				
Wheat	11	27	0.662	0.416
Soy	23	30	0.030	0.862
Barley	17	24	2.575	0.109
Rice	18	21	0.306	0.580
Dairy products				
Cow milk	30	53	0.043	0.836
Fruits				
Banana	15	38	1.090	0.296
Grapes	26	36	2.176	0.140
Kiwi	39	51	0.613	0.434
Strawberry	10	28	0.662	0.416
Cantaloupe	37	44	0.776	0.378
Watermelon	12	44	2.734	0.098
Meat				
Beef	30	74	1.938	0.164
Mutton	16	26	2.886	0.089
Chicken	10	23	1.650	0.199
Shrimp	29	43	1.212	0.271
Fish	18	31	0.043	0.835
Nuts				
Walnut	27	49	1.212	0.271
Hazelnut	26	44	0.018	0.893
Almond	18	37	0.189	0.663
Peanut	41	62	1.136	0.287
Carbonated beverages				
Sausages	49	71	0.297	0.586
Canned food	53	75	0.757	0.384
Coffee	43	53	1.219	0.270
Traditional cheese	39	55	0.333	0.564
Industrial cheese	28	44	0.045	0.832
Cocoa	29	40	0.185	0.667

**Table 5.** Evaluation of the Relationship Between the Triggering Potential of Foodstuffs on the Initiation and Exacerbation of Migraine Based on Age

Foodstuff	Impact on Migraine		Mann-Whitney Test	P Value
	Average Age			
	Negative	Positive		
Egg	28.85	36.48	-1.629	0.103
Cereals				
Wheat	32.54	29.32	-0.535	0.593
Soy	31.82	32.57	-0.137	0.891
Barley	32.13	31.46	-0.114	0.909
Rice	31.71	33.36	-0.272	0.786
Dairy products				
Cow milk	34.63	27.09	-1.559	0.119
Fruits				
Banana	30.86	35.63	-0.881	0.378
Grapes	29.89	37.71	-1.504	0.133
Kiwi	32.00	32.00	0.000	1.000
Strawberry	32.36	30.32	-0.33-	0.737
Cantaloupe	30.16	35.43	-1.090	0.276
Watermelon	31.22	34.50	-0.606	0.545
Meat				
Beef	29.86	34.68	-1.039	0.299
Mutton	31.69	33.33	-0.280	0.779
Chicken	31.39	35.25	-0.612	0.540
Shrimp	28.96	38.07	-1.862	0.063
Fish	30.31	37.93	-1.374	0.169
Nuts				
Walnut	31.52	32.95	-0.29-	0.770
Hazelnut	30.94	34.45	-0.697	0.486
Almond	30.09	38.10	-1.479	0.139
Peanut	30.76	33.45	-0.580	0.562
Carbonated beverages				
Sausages	31.05	32.81	-0.380	0.704
Canned food	27.00	36.00	-1.939	0.052
Coffee	30.86	33.62	-0.58-	0.557
Traditional cheese	32.03	31.96	-0.014	0.989
Industrial cheese	32.14	31.70	-0.089	0.929
Cocoa	31.13	34.03	-0.577	0.564

allergic to shrimp experience headaches less frequently.

The scratch test is most commonly used to justify the relationship between allergen foods and primary headaches (9), and an elimination diet is then recommended based on the results. Most studies in this regard have reported a relatively high success rate.

There were other triggers as well (34.4%). Ultimately, it was concluded that migraine triggers among Indians were the same as those for other populations; however, they were mostly linked with dietary factors (10). According to the report of Wöber et al, knowledge of dietary stimulants for migraine would decrease their frequency

of consumption (11).

In the same study, Yadav et al considered wine, chocolate, fruits, and vegetables ( $P < 0.05$ ) as the stimuli reported by patients with migraine and tension headaches. However, hunger was an exception since the personal experience was more extensive than theoretical knowledge in this regard (12-19).

Immunological mediators such as IgE and histamine tumor necrosis factor (TNF-alpha), calcitonin gene-dependent peptide, intestinal vasoactive peptide, prostaglandins D2 and F2, interleukin 1, and tryptase,

**Table 6.** Evaluation of the Relationship Between the Triggering Potential of Foodstuffs on the Initiation and Exacerbation of Migraine Based on Patients' Headache Hours During a Day

Foodstuff	Impact on Migraine		Mann-Whitney Test	P Value
	Average Rank of Pain Hours			
	Negative	Positive		
Egg	30.91	33.56	-0.572	0.567
Cereals				
Wheat	32.53	29.50	-0.504	0.614
Soy	34.03	23.38	-1.833	0.067
Barley	33.13	26.68	-1.071	0.284
Rice	32.53	29.50	-0.504	0.614
Dairy products				
Cow milk	32.18	31.66	-0.109	0.913
Fruits				
Banana	32.60	30.07	-0.473	0.636
Grapes	33.51	27.91	-1.089	0.276
Kiwi	32.11	31.84	-0.057	0.955
Strawberry	32.36	30.32	-0.339	0.735
Cantaloupe	30.04	35.66	-1.174	0.240
Watermelon	33.21	28.13	-0.947	0.344
Meat				
Beef	28.83	35.96	-1.553	0.120
Mutton	33.37	26.17	-1.239	0.215
Chicken	33.19	25.70	-1.199	0.231
Shrimp	29.30	37.40	-1.674	0.094
Fish	32.95	28.68	-0.778	0.437
Nuts				
Walnut	31.90	32.19	-0.059	0.953
Hazelnut	32.64	30.53	-0.424	0.671
Almond	33.03	28.70	-0.808	0.419
Peanut	33.87	29.81	-0.886	0.376
Carbonated beverages				
Sausages	33.66	30.67	-0.651	0.515
Canned food	32.16	31.77	-0.085	0.932
Coffee	32.81	30.85	-0.424	0.672
Traditional cheese	36.41	22.53	-2.831	0.005
Industrial cheese	35.65	23.55	-2.432	0.015
Cocoa	33.20	29.60	-0.745	0.456

**Table 7.** Evaluation of the Relationship Between the Triggering Potential of Foodstuffs on the Initiation and Exacerbation of Migraine Based on the Monthly Frequency of Headaches

Foodstuff	Impact on Migraine		Mann-Whitney Test	P Value
	Average Number of Headache			
	Negative	Positive		
Egg	31.45	32.79	-0.290	0.772
Cereals				
Wheat	32.12	31.45	-0.110	0.912
Soy	33.00	28.80	-0.784	0.433
Barley	33.19	26.96	-1.072	0.284
Rice	31.96	32.18	-0.037	0.971
Dairy products				
Cow milk	32.30	31.43	-0.182	0.855
Fruits				
Banana	32.81	29.40	-0.637	0.524
Grapes	31.36	33.74	-0.462	0.644
Kiwi	32.03	31.96	-0.014	0.989
Strawberry	32.33	30.45	-0.312	0.755
Cantaloupe	30.23	35.30	-1.058	0.290
Watermelon	31.75	32.80	-0.947	0.344
Meat				
Beef	35.41	27.73	-1.673	0.094
Mutton	31.00	36.25	-0.904	0.366
Chicken	31.34	35.50	-0.666	0.505
Shrimp	28.81	38.38	-1.977	0.048
Fish	32.18	31.36	-0.151	0.880
Nuts				
Walnut	31.21	33.57	-0.487	0.626
Hazelnut	33.90	27.61	-1.266	0.206
Almond	31.84	32.50	-0.123	0.903
Peanut	29.72	34.67	-1.082	0.279
Carbonated beverages	31.52	32.41	-0.195	0.845
Sausages	35.07	29.54	-1.204	0.229
Canned food	31.91	32.13	-0.049	0.961
Coffee	35.43	27.12	-1.795	0.073
Traditional cheese	33.74	28.25	-1.121	0.262
Industrial cheese	34.31	26.66	-1.539	0.124
Cocoa	30.76	34.48	-0.767	0.443

as well as most cell activation and nitric oxide secondary release, were observed in both migraine and allergy (13).

Moreover, migraine patients considered variations in weather (83%), season change (75%), and exposure to allergens (62%) as headache triggers (7). In another study in a rhinology tertiary care center, Perry et al found that the incidence of migraine was 58% among patients with headaches who had normal radiology and endoscopic findings (14). Ku et al evaluated individuals who were above 40 years of age and had a positive radioallergosorbent test, at least one of the common inhaled allergens, and at

least two positive answers to the 6 questions regarding AR (nasal congestion, rhinorrhoea, sneezing, snoring or mouth breathing, pharyngeal discharge, and itchy and watery eyes). The other investigated individuals in their study had one of the symptoms of AR on examination (pale or swollen turbinates, mucous secretions in the nasopharynx airways, dark rings around the eyes, and the backline of the nose). The control group included non-atopic patients who had been referred to internal medicine and pediatric clinics (15).

A meta-analysis in 2001 reviewed studies conducted between 1996 and 1999 on the relationship between migraine and immune system function. It was concluded that the impact of the immune system on intensifying migraine headaches due to the potential impact of atopic disorders on migraine is still debatable. Since 1996, about 45 studies considered immune system function changes in migraine patients; they were all reviewed by Kemper et al. The variations of serum complement levels and immunoglobulins, histamine, cytokines, and immune cells have been identified in some of these studies, but have not been confirmed in most cases. The above-mentioned study demonstrated that there is no definite proof for immune function disorders in migraine. Nonetheless, the likelihood of this relationship is not ruled out totally. The variations in the findings are partly due to the differences in the sampling methods linked with the timing of migraine attacks. In this regard, the findings of this study represented that sampling times should be precisely defined based on immune system function in migraine patients (16). Pradalier and Launay studied the immunological aspects of migraine and observed alterations in immunoglobulins, especially IgE, complement function, mediators, cytokines, and inflammatory cells. However, conclusive remarks about the role of the immune system in the pathophysiology of migraine are assigned for further studies (17).

Özge et al examined 186 migraine cases for the relationship between migraine and atopic diseases in the department of neurology of a university in Turkey. They concluded that 41.4% of migraine patients had at least one atopic disorder, which may indicate a positive relationship between such disorders and migraine headaches (18). Evidently, different studies expressed varied findings regarding the relationship between migraine and allergens, along with the impact of the immune system on migraine. The measurement time of the immune system factors, study groups, and headache time would explain the discrepancies in the findings. For instance, in some studies, the measurement time was during the intervals between migraine attacks, while in other studies, it was at the onset of the attack. In other cases, the measurement time was not defined at all. On the other hand, some studies selected their control group from healthy individuals, while in others, patients with

headaches other than migraine were included in the control group. Moreover, the medical condition of atopic disorders could have affected the severity of migraine and its relationship with allergens.

Research has identified different causes of migraine, including foods, stress, depression, anxiety, hormones, barometric pressure, light, cigarette smoking, and headache medications. However, the researchers have not yet figured out how to determine the specific etiology of headaches. Those who study migraine and diet mostly face problems such as the headaches which develop after eating a triggering substance but are actually the result of other substance deposits. The other reason for the inconsistency of findings in migraine studies is their lack of definite diagnostic criteria. Most of them simply claim that the participant had been diagnosed with migraine without stating the applied diagnostic criteria. The third underlying reason for the incompatibility in such studies would be their lack of or indefinite participant inclusion criteria, which would be absolutely misleading. The fourth explanation for divergent results is the methodological differences. In the studies with blinding methods, the given dose, number of administered doses, and measurements were different. In some cases, insufficient information regarding the methods expanded the ambiguities. Last but not least, some authors' reluctance to use inferential statistics for data analysis increase the obscurity. Although inferential statistics lead to more definitive conclusions, only a few studies take this advantage.

It is evident that the methodology is directly impacted by the intention of the study. A challenging study should be performed given that the goal of a project is to evaluate a biochemical mechanism associated with food. However, a therapeutic study must be conducted if the intention is treatment. It is recommended that research on therapies should be performed through double blinding rather than non-blind eating challenges. Accordingly, any impact could be easily attributed to the foodstuff per se instead of other non-specific factors.

Although diet-induced migraine is a common phenomenon that affects many people, it is not yet fully clarified which foodstuff becomes a trigger or under which conditions they change. Learning to detect migraine-triggering foods and the influencing conditions, as well as identifying susceptible individuals leads to effective headache management. For future studies, it is suggested that the present project be modified with more participants. Furthermore, through intervention and elimination of allergens from individuals' diets, the role of specific allergens could be clarified more accurately. It is high time that we take actions to prevent disease through changing people's lifestyles.

#### Acknowledgments

Hereby, the authors would like to express their gratitude to all the people who enthusiastically devoted their time and energy to

accomplishing this project, especially the patients who enduringly took their time to fill out the questionnaires.

This paper was extracted from a thesis for the degree of general practice at Hormozgan University of Medical Sciences. The deputy of research deserves appreciation as well.

#### Authorship Contributions

Conceptualization: AN, Methodology: AN; Validation: AN; Formal Analysis: SHT; Investigation: AT; Resources: AT; Data Curation: BA ; Writing—Original Draft Preparation:AT, AP; Writing—Review and Editing:AT, AP; Supervision:AN; Project Administration:AN.

#### Conflict of Interests

The authors hereby declare that there was no conflict of interests for this project, and all funding was handled by themselves

#### Ethical Approval

This study received ethical approval from the Ethics Committee of Hormozgan University of Medical Sciences (IR.HUMS.REC.1399.513).

#### References

- Silberstein SD, Lipton RB, Dalessio DJ. *Wolf's Headache and Other Head Pain*. Oxford: Oxford University Press; 2001.
- Mitchell N, Hewitt CE, Jayakody S, Islam M, Adamson J, Watt I, et al. Randomised controlled trial of food elimination diet based on IgG antibodies for the prevention of migraine like headaches. *Nutr J*. 2011;10:85. doi: [10.1186/1475-2891-10-85](https://doi.org/10.1186/1475-2891-10-85).
- Alpay K, Ertas M, Orhan EK, Ustay DK, Lieners C, Baykan B. Diet restriction in migraine, based on IgG against foods: a clinical double-blind, randomised, cross-over trial. *Cephalalgia*. 2010;30(7):829-37. doi: [10.1177/0333102410361404](https://doi.org/10.1177/0333102410361404).
- Wallace DV, Dykewicz MS, Bernstein DI, et al. The diagnosis and management of rhinitis: an updated practice parameter [published correction appears in *J Allergy Clin Immunol*. 2008 Dec;122(6):1237]. *J Allergy Clin Immunol*. 2008;122(2 Suppl):S1-S84. doi:[10.1016/j.jaci.2008.06.003](https://doi.org/10.1016/j.jaci.2008.06.003).
- Hanington E. Diet and migraine. *J Hum Nutr*. 1980;34(3):175-80. doi: [10.3109/09637488009143438](https://doi.org/10.3109/09637488009143438).
- Masoud SA, Ehteram H. Relationship between serum IgE level and migraine headache. *Feyz*. 2008;12(1):44-9. [Persian].
- Rosario D, Pinto G. Role of gender and serum immunoglobulin E (IGE) levels on severity of migraine. *J Clin Diagn Res*. 2014;8(2):57-8. doi: [10.7860/jcdr/2014/7516.4007](https://doi.org/10.7860/jcdr/2014/7516.4007).
- Saberi A, Nemati S, Jafari Shakib R, Kazemnejad E, Maleki M. Association between allergic rhinitis and migraine. *J Res Med Sci*. 2012;17(6):508-12.
- Wise SK, Lin SY, Toskala E, Orlandi RR, Akdis CA, Alt JA, et al. International consensus statement on allergy and rhinology: allergic rhinitis. *Int Forum Allergy Rhinol*. 2018;8(2):108-352. doi: [10.1002/alr.22073](https://doi.org/10.1002/alr.22073).
- Sulena, Singla M, Brar J, Kale R, Kale S. Clinical profile of migraine in a rural population presenting to tertiary care hospital in North India. *Ann Indian Acad Neurol*. 2020;23(6):781-6. doi: [10.4103/aian.AIAN\\_671\\_19](https://doi.org/10.4103/aian.AIAN_671_19).
- Wöber C, Holzhammer J, Zeitlhofer J, Wessely P, Wöber-Bingöl C. Trigger factors of migraine and tension-type headache: experience and knowledge of the patients. *J Headache Pain*. 2006;7(4):188-95. doi: [10.1007/s10194-006-0305-3](https://doi.org/10.1007/s10194-006-0305-3).
- Nowaczewska M, Wiciński M, Kaźmierczak W, Kaźmierczak H. To eat or not to eat: a review of the relationship between chocolate and migraines. *Nutrients*. 2020;12(3):608. doi:

- 10.3390/nu12030608.
13. KGazerani P, Pourpak Z, Ahmadiani A, Hemmati A, Kazemnejad A. A correlation between migraine, histamine and immunoglobulin e. *Scand J Immunol.* 2003;57(3):286-290. doi:10.1046/j.1365-3083.2003.01216.x.
  14. Perry BF, Login IS, Kountakis SE. Nonrhinologic headache in a tertiary rhinology practice. *Otolaryngol Head Neck Surg.* 2004;130(4):449-52. doi: 10.1016/j.otohns.2004.01.005.
  15. Ku M, Silverman B, Prifti N, Ying W, Persaud Y, Schneider A. Prevalence of migraine headaches in patients with allergic rhinitis. *Ann Allergy Asthma Immunol.* 2006;97(2):226-30. doi: 10.1016/s1081-1206(10)60018-x.
  16. Kemper RH, Meijler WJ, Korf J, Ter Horst GJ. Migraine and function of the immune system: a meta-analysis of clinical literature published between 1966 and 1999. *Cephalalgia.* 2001;21(5):549-57. doi: 10.1046/j.1468-2982.2001.00196.x.
  17. Pradalier A, Launay JM. Immunological aspects of migraine. *Biomed Pharmacother.* 1996;50(2):64-70. doi: 10.1016/0753-3322(96)84715-9.
  18. Özge A, Uluduz D, Bolay H. Co-occurrence of migraine and atopy in children and adolescents: myth or a casual relationship? *Curr Opin Neurol.* 2017;30(3):287-91. doi: 10.1097/wco.0000000000000439.
  19. Yadav RK, Kalita J, Misra UK. A study of triggers of migraine in India. *Pain Med.* 2010;11(1):44-7. doi: 10.1111/j.1526-4637.2009.00725.x.