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RESEARCH ARTICLE

The Frequency of Food Allergy Among Children With Migraine Headache; A Descriptive Cross-Sectional Study

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Abstract:

Background:

Headache and particularly migraine headaches are considered as a debilitating disease worldwide that can adversely affect the quality of life of children and adults. Various factors can play a critical role in the development of migraine headache attacks. The food allergens are considered as important factors. This study aimed to determine the frequency of food allergy in children with migraine headaches.

Methods:

Forty patients aged <16 years with a migraine headache were entered into the study. A questionnaire was provided in which data on demographic information and skin test results for various allergens were recorded. Dietary allergies were defined based on a positive skin test plus a patient's history of food allergies. The severity of migraine was evaluated using the Migraine disability assessment score (MIDAS) questionnaire.

Results:

The present study showed 32.5% of our participants had a food allergy. No significant association was detected between sex (p=58) and age (p=0.14) with food allergy. However, the frequency of food allergy was significantly higher in patients aged ≥12 years old (44.4%) than those aged <12 (22.7%). A significant relationship was found between the number of attacks after prophylaxis and the frequency of food allergies (p=0.032). Individuals with lower attacks had a lower food allergy.

Conclusion:

Our findings revealed that about one-third of children with a migraine headache had a food allergy. This frequency was significantly higher in children with migraines than that of the general population based on the results of previous studies. It is recommended that these patients receive a skin allergy test while preparing a strong history of food allergies or when the frequency of migraine attacks does not decrease significantly despite proper prophylaxis.

Keywords: Children is a common word, Food allergy, Migraine, Headache, PRICK test, Pediatric.

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1. INTRODUCTION

Migraine headaches are a debilitating condition that diminishes the quality of life in both adults and children. Migraine headaches are common in children and have a variety of clinical symptoms [1]. Clinically, it is significantly affected by nutritional and gastrointestinal issues, which are correlated to the consumption of certain stimulants and food allergens such as dairy and gluten [2].

The incidence of food allergy and nutritional intolerance has been increased in recent years, which may be due to less exposure to bacterial agents [3]. The risk of migraine in asthma patients is 1.45 times higher than in non-asthmatic individuals [4]. Food allergies are caused by the responses of the immune system to foods [5]; however, it is different from food intolerance as it is caused by enzymatic disturbances and

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occurs after the consumption of certain foods [5, 6].

Recent research has shown the level of histamine is possibly involved in allergies and migraines [7]. Daily diet program can perform an important role in the frequency of headaches in children and adolescents with migraine. The dietary factor in pediatric migraine is often overlooked because of treatment with preventive drugs. Chocolate, cheese, fatty foods, hot dogs, ice cream, monosodium glutamate, citrus, aspartame, caffeine and alcoholic beverages, especially red wine and beer are the most common foods, beverages and additives that trigger migraines [7 - 9]. Alcohol consumption is another potential cause of recurrent headache in younger individuals [10]. Tyramine, phenylethylamine, histamine, nitrite and sulfides are considered as the possible mediators for headaches caused by food intolerance [11, 12]. Some studies revealed that diets are effective in migraine attacks by affecting the release of serotonin and norepinephrine that subsequently cause vasoconstriction or vasodilatation or by direct stimulating of the trigeminal ganglion, brainstem and cortical-neuronal pathways [7, 13].

Regarding the association between different foods intake and the incidence of migraine and headache in allergic patients, the determination of hypersensitivity to common allergens in these patients is very important to establish a preventive program to reduce patient's exposure to these agents. Therefore, this study was designed to evaluate the prevalence of food allergy in children with migraines who were referred to the pediatric neurology clinic of Ayatollah Mousavi Hospital in 2016 and 2017.

2. MATERIALS AND METHODS

In this descriptive cross-sectional study, all children with migraine headaches and aged under 16 years old who referred to the pediatric Neurology Clinic of Ayatollah Mousavi Hospital during 2016-2017 were entered. This study was approved by the Ethics Committee of Zanjan University of Medical Sciences. Dietary allergies were defined based on a positive skin test plus a patient's history of food allergies. The diagnosis of migraine was provided by a pediatric neurologist based on migraine criteria. The severity of the disease was assessed by the Migraine Disability Assessment Scale (MIDAS) questionnaire. A checklist was provided and information on demographic data, type of allergy, and migraine headache characteristics was recorded.

The skin test was performed using the acupuncture technique. In this method, a small drop of the desired allergen extract was placed on the surface of the skin in areas that had been pre-identified by numbering. A slight scratch was provided with a small needle head and a small amount of the allergen extract was transferred into the epidermis of the outer layer of the skin. Positive (H) and negative (C) control skin tests were performed using histamine and saline, along with selected allergens (Fig. **1**). The negative control test was performed for the assessment of dermatographism or reactions caused by pressures on sensitive skin, while the positive control test was provided to prove a dermal response to histamine. Antigenic extracts used in this study included tree, grass, weed, beetle, mite, *Alternaria*, *Aspergillus*, tomato, egg, shrimp, beef, chocolate, milk, almond, pepper and walnut. The PRICK TO PRICK test was carried out for almond, pepper and walnut. The extracts were purchased from Greer Company (USA). The skin test result was read 15 minutes after the extracts were poured onto the skin and based on the amount of induration and erythema created. Thus, a diameter above 10 mm and an induration diameter above 3 mm were considered as positive tests. However, the presence of either induration or erythema was sufficient to be positive. It is also a positive skin test. A positive reaction to an allergen is also considered a positive skin test.

3. STATISTICAL ANALYSIS

All quantitative data were analyzed using the descriptive program and presented as Mean ± SD. Crosstabs and Chi-Square tests were used to compare the percentage or frequency of parameters between the two groups. The comparison of the mean of parametric and normalized data between two groups was analyzed using an independent student sample t-test. Mann-Whitney test was applied in the case of non-normal data. In this study, $p< 0.05$ was considered statistically significant. The SPSS software (IBM, version 18) was applied for data analysis.

4. RESULTS

A total of 40 cases with a mean age of 10.90 ± 2.48 years were enrolled in the study. The results of the basic demographic and clinical findings of all cases are summarized in Table **1**. The percentage of patients less than 12 years old and older than 12 years old was 45% (18 cases) and 55% (22 cases), respectively. Twenty-four patients (60%) were boys and 16 cases (40%) were girls. The frontal was the most commonplace of headache in these patients (45%). In most cases (80%), the headache was bilateral. While 32.5% of patients had mild to moderate disease, 67.5% of cases had severe disease. In most cases (77.5%), the headache was throbbing, and 67.5% of patients also suffered from headaches during activity. Motion sickness was found in 32.5% of cases. The time interval between attacks before beginning migraine prophylaxis in more than half of patients (55%) was <1 week, while 37.5% of whom had a time interval between attacks 1 week to 1 month. The time interval between attacks after beginning migraine prophylaxis in most patients (45%) was 1 month to 3 months and 37.5% of patients had 1 week to 1 month (Table **1**).

The frequency of food allergies, according to the characteristics of migraine attacks, is shown in Table **2**. Overall, 32.5% of patients had food allergies (13 out of 40 children). The incidence of food allergies in children under 12 was 22.5% (5 out of 22), while it was 44.4% (8 out of 18) in children ≥12 years old ($p=0.14$). The incidence of food allergies in boys and girls was 29.2% (7 out of 24) and 37.5% (6 out of 16), respectively ($p=0.58$). A significant relationship was found between the number of attacks after prophylaxis and the frequency of food allergies ($p=0.032$).

Fig. (1). The initiation of being a positive skin test in a case.

Table 1. The basic demographic and clinical characteristics of patients.

Variables	Results
Age (Month)	10.90 ± 2.48
Age groups	
≥12 years (%)	22 (55%)
<12 years (%)	18 (45%)
Gender	
Boys (%)	24 (60%)
Girls (%)	16 (40%)
Headache zone	
Vertex (%)	7 (17.5%)
Occipital (%)	8 (20%)
Frontal (%)	18 (45%)
Temporal (%)	7 (17.5%)
Unilateral/bilateral	
Unilateral (%)	8 (20%)
Bilateral (%)	32 (80%)
Disease severity	
Mild to moderate (%)	13 (32.5%)
Severe (%)	27 (67.5%)
Headache quality	
Throbbing (%)	31 (77.5%)
Non-throbbing (%)	9 (22.5%)
Headache coupled with activity	
Yes (%)	27 (67.5%)
No (%)	13 (32.5%)
Motion sickness	
Yes (%)	13 (32.5%)
No (%)	27 (67.5%)
Attacks before beginning prophylaxis	
<1 week	22 (55%)
1 week to 1 month	15 (37.5%)
1 month to 3 month	3 (7.5%)
>3 month	0
Attacks after beginning prophylaxis	
<1 week	1 (2.5%)
1 week to 1 month	15 (37.5%)
1 month to 3 month	18 (45%)
>3 month	6 (15%)

Table 2. The frequency of food allergies according to the characteristics of migraine attacks.

Type of headache	Food allergy	p-value
Headache zone		
Vertex (%)	2 (28.6%)	0.67
Occipital (%)	3 (37.5%)	
Frontal	7 (38.9%)	
Temporal	1 (14.3%)	
Unilateral/bilateral		
Unilateral (%)	1 (12.5%)	0.17
Bilateral (%)	12 (37.5%)	
Disease severity		
Mild to moderate (%)	4 (30.8%)	0.87
Severe (%)	9 (33.3%)	
Headache quality		
Throbbing (%)	1 (35.5%)	0.45
Non-throbbing (%)	9 (100%)	
Headache coupled with activity		
Yes (%)	9 (33.3%)	0.87
No (%)	4 (30.8%)	
Motion sickness		
Yes (%)	4 (30.8%)	0.87
No (%)	9 (33.3%)	
Attacks before prophylaxis		
<1 week	9 (40.9%)	0.30
1 week to 1 month	4 (26.7%)	
1 month to 3 month	0	
>3 month	0	
Attacks after prophylaxis		
<1 week	1 (100%)	0.032
1 week to 1 month	8 (53.3%)	
1 month to 3 month	4 (22.2%)	
>3 month	0	

In this study, 70% of children had positive skin tests (28 out of 40). The prevalence of positive skin tests in children <12 years old was 63.6% (14 out of 22), while it was 77.8% (14 out of 18) in children ≥12 years old (p= 0.332). The frequency of positive skin tests in boys and girls was 75% (18 out of 24) and 62.5% (10 out of 16), respectively (p=0.39). Table **3** shows the frequency of positive skin tests in terms of the characteristics of migraine attacks. The results showed no significant relationship between the characteristics of migraine attacks and positive skin tests.

Table **4** shows the frequency of people with migraine who had a positive allergen skin test. The results showed that grass (45%) and weed (40%) were the most common type of allergens among patients with a positive skin test. The frequency of tree and beetle in cases with a positive skin test was 22.5% and 15%, respectively.

5. DISCUSSION

In this study, we investigated the prevalence of food allergies among children with migraines. Our findings revealed that approximately one-third of the patients had food allergies. There was no significant association between sex and age with food allergies; however, the frequency of food allergies was significantly higher in children ≥12 years of age. While the prevalence of food allergies in children <12 years was 22.7%, it was 44.4% in children ≥12 years.

Table 3. The frequency of positive skin test based on migraine attack characteristics.

Type of headache	Positive skin test	p-value
Headache zone		
Vertex (%)	5 (71.4%)	0.062
Occipital (%)	6 (75.0%)	
Frontal	15 (83.3%)	
Temporal	2 (28.6%)	

(Table 3) cont.....

Type of headache	Positive skin test	p-value
Unilateral/bilateral		
Unilateral (%)	5 (62.5%)	0.67
Bilateral (%)	23 (71.9%)	
Disease severity		
Mild to moderate (%)	11 (84.6%)	0.16
Severe (%)	17 (63.0%)	
Headache quality		
Throbbing (%)	5 (55.6%)	0.28
Non-throbbing (%)	23 (74.2%)	
Headache coupled with activity		
Yes (%)	19 (70.4%)	0.94
No (%)	9 (69.6%)	
Motion sickness		
Yes (%)	8 (61.5%)	0.41
No (%)	20 (74.1%)	
Attacks before prophylaxis		
Every week	16 (72.7%)	0.35
1 week to 1 month	9 (60%)	
1 month to 3 month	3 (100%)	
>3 month	0	
Attacks after prophylaxis		
Every week	1 (100%)	0.32
1 week to 1 month	12 (80%)	
1 month to 3 month	10 (55.6%)	
>3 month	5 (83.3%)	

Table 4. The frequency of people with migraine and positive skin test based on the type of allergen.

Type of allergen	Frequency
Tree	9 (22.5%)
Grass	18 (45%)
Weed	16 (40%)
Beetle	6 (15%)
Mite	4 (10%)
Alternaria	0
Aspergillus	0
Tomato	1 (2.5%)
Egg	1 (2.5%)
Shrimp	2 (5%)
Beef	0
Chocolate	1 (2.5%)
Cow milk	2 (5%)
Pepper	3 (7.5%)
Almonds	1 (2.5%)
Walnuts	0

Pourpak *et al.* [14] evaluated common food allergens in Iranian Children. Skin prick test was performed in 171 patients (all patients, except those with severe eczema, negative response to positive control or severe dermo-graphism). Skin prick test was positive in 53.2% of children. They pointed out that the incidence of food allergy in children is higher than adults and mentioned that up to 8% of children less than 3 years of age and 2% of adults suffer from food allergy.

Zang *et al.* [15] evaluated the prevalence of food allergies in the general population of children aged 3 to 12 years from 9 areas of China. They reported that the prevalence of food allergies among this population was 8.4%. In another study in the USA, Gupta *et al.* [16] reported that the prevalence of food allergies in the normal population of children was 8%. Hoyos-Bachiloglu *et al.* [17] reported that the incidence of food allergies in the pediatric population from Santiago was 5.5%.

According to these accomplished data, our finding indicates that the prevalence of food allergies in children with migraines is significantly greater than the general pediatric population. Similarly, Mansfield *et al.* [18] considered the incidence of food allergies in adults with migraine, and found that the prevalence of food allergies in these patients is 37.5%, which is consistent with the finding of our study. However, they considered food allergies in adult patients and positive skin tests were evaluated using at least 85 nutrients.

The results of our study also showed that the prevalence of food allergies in children aged ≥12 years old was significantly higher than in children <12 years old. This result can be somewhat predictable. The immune system develops along with age, resulting in a stronger immune response to existing allergens such as food allergies. On the other hand, it is possible that children will be exposed to different allergies as they get older and experience various diets. Furthermore, the frequent contacts of older children with other individuals can be effective in stimulating their immune system and may increase the prevalence of allergies in persons aged ≥12 years old compared to those <12 years old.

We also observed that among the potential allergens studied, pepper, milk, shrimp, and eggs, as well as tomatoes, almonds and chocolate were the only foods that some children were allergic to them. A study in China identified fish and other seafood, milk and fruit as the most important allergens in the general pediatric population [15]. It should be, however, noted that many potential allergen foods have not been evaluated in the present study, and it is possible a varied list of food allergens may be introduced as the list of allergens increased. However, the differences in food allergies (in terms of allergies to the type of food consumed) can be largely influenced by the different food cultures in different communities.

Our findings also revealed that the prevalence of food allergies was decreased, both before and after the beginning of migraine prophylaxis, with a decrease in the number of migraine attacks. However, this decrease was significant after the beginning of migraine prophylaxis. This finding indicates that the number of attacks can be correlated to food sensitivity because some allergenic foods trigger migraines. On the other hand, there is a significant decrease in food sensitivity by reducing the number of migraine attacks after the beginning of migraine prophylaxis *versus* non-significant reduction in the number of them before prophylaxis. It may be referred to some prophylactic medications used in migraine, which primarily emphasize anti-allergic prophylaxis. We used of Cinnarizine (½ Tab QHS) in our patients that have anti-allergic effects. The use of common prophylactic drugs such as tricyclic and beta-blockers has no anti-allergic properties and as a result, their use in cases where a migraine is triggered by food allergens is not prevented. As a result, the role of food stimulants and allergens in triggering attacks can become more highlighted.

Interestingly, our results revealed that 70% of the patients were positive for a skin test. Evaluation of common food allergens in Iranian Children reported that the prevalence of the positive skin tests was 53.2% of children [14. The 3rd survey of 10 common allergens in the US general health and nutrition examinations reported that the prevalence of the positive skin test was 54% (19). However, this study was conducted among individuals aged from 6 to 59 years old. The prevalence of the positive skin test was 45.6% in 6- to 9-year-old children, while it was 55.5% in 10- to 19-year-old individuals [19]. This is approximately 15%-20% lower than that reported in our study. However, it should be noted that the number and type of allergens examined in our study were different from this study. A study in Europe reported that the positive skin test was 8% to 30% [20, which is much lower than that estimated in our study population. This may indicate the association of migraine with allergies. Additionally, our patients had the highest hypersensitivity to grass. Although these estimates in our study were significantly higher than the general population reported by previous studies, differences in the frequency of positive skin tests can depend on various factors, such as race, the population of the study, and other demographic characteristics. More importantly, the number of allergens and the type of allergens can play an important role in estimating these frequencies.

One of the limitations of this study is related to the low sample size, which can affect the ability of the study to detect differences or determine significant relationships. However, the main purpose of this study was to determine the frequency of food allergy in people with migraine. The other limitations of this study are the lack of skin testing for many food allergens that could influence the frequency of food allergies. However, the skin test is not usually an easy task for all allergens.

CONCLUSION

Our study showed that 70% of children with migraine headaches had a positive skin test result. Furthermore, about one-third of children with migraine have suffered from food allergies, which is significantly higher than the general population according to past studies. Therefore, identification and consideration of food allergens in children with a migraine headache are essential. Given the high frequency of food allergies in children with migraine headaches, it is recommended that these patients receive a skin allergy test while preparing a strong history of food allergies or when the frequency of migraine attacks does not decrease significantly despite proper prophylaxis. However, further studies with larger sample size and a wide range of food allergens are helpful.

AUTHORS' CONTRIBUTIONS

Akefeh Ahmadiafshar and Mohammad Vafaee-Shahi designed and managed the study. Fariba Khosroshahi analyzed and interpreted the patients' data and performed follow-up of the patients, Saeide Ghasemi and Aina Riahi were major contributors in writing the manuscript. All of the authors read and approved the final manuscript.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

This study was approved by the Ethics Committee of Zanjan University of Medical Sciences. The ethical number was ZUMS.REC.1395.234.

HUMAN AND ANIMAL RIGHTS

Not Applicable.

CONSENT FOR PUBLICATION

The consent for publication of personal detailed data was obtained from parents.

AVAILABILITY OF DATA AND MATERIAL

The datasets used during the current study are available from the corresponding author [A.A] on a reasonable request.

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None declared.

CONFLICT OF INTEREST

The authors declares no conflict of interest, financial or otherwise.

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