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Role of Food Allergy in Development of Different Levels of Asthma Severity in Childhood

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Abstract

Background

Various risk factors, including previous history of food allergy, may play an important role in predicting the development and the outcome of asthma in children. This study aims to assess the relationship of previous food allergy in infancy with asthma severity later in childhood.

Materials and Methods: Infants and children of up to 14 years of age referred to the Allergy Clinics of Azad University Hospitals in Tehran, Iran from October 2018 to October 2019 due to asthma were enrolled in this cross-sectional study. After confirming the diagnosis by a specialist physician and determining the level of severity, the patients' caregivers were asked to fill out an eight-item researcher-made questionnaire. The questionnaire focused on family and the child's history of allergy, specifically a previous history of clinically diagnosed food allergy.

Results: A total of 170 asthmatic patients with a mean age of 7.1±3 years were enrolled in the study. A meaningful relationship was found between food allergy and asthma ($p < 0.001$). Also, there was a significant relationship between having a history of food allergy in children with moderate and severe asthma compared to those with mild asthma ($p<0.001$). However, no such meaningful relationship was found when comparing moderate and severe asthma ($p=0.6$).

Conclusion

The findings suggested that food allergy in conjunction with a positive family history is a risk factor for persistent problematic asthma, which places patients at greater risk of morbidity. A history of previous food allergy was significantly associated with moderate to severe asthma compared to mild asthma.

Key Words: Asthma, Children, Food allergy, Severity.

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1- INTRODUCTION

Atopic march or allergic march is a well-known term denoting the development and progression of atopic diseases, including food allergy, eczema, asthma, and allergic rhinitis during childhood and adolescence (1). The prevalence of food allergy has increased in recent decades (2, 3). Although a real estimation of the food allergy prevalence has been difficult to obtain at times (4). Many children outgrow their food allergies (4), however, it has been shown that early-life food sensitization is a strong predicator of the chance of developing asthma later in the childhood (5, 6) and its severity (7). Asthma is one of the most common conditions and affects approximately 9% of children worldwide (8). Because of the diverse phenotypes of asthma in children with transient and persistent wheezing, different risk factors, including allergic diseases (e.g., food allergy, viral (9), or bacterial respiratory infections during the first years of life, and reduced lung function (10)) may play an important role not only in establishing the diagnosis of asthma but also in predicting the outcome of the disease in children.

Asthma and food allergy are both complex conditions that share similar risk factors. Many previous studies have shown the role of food allergies in later development of asthma in children (11). It has been previously estimated that 50% of children with food allergy may later develop respiratory symptoms and 4-8% of asthmatic patients have a previous history of food allergy (10). Therefore, food allergy is a risk factor for persistent problematic asthma, which places patients at greater risk for morbidities. This study aims to evaluate the relationship between previous food allergy in infancy and later development of varying levels of asthma severity in childhood.

2- MATERIALS AND METHODS

2-1. Study design and population

All infants and children of up to 14 years of age referred due to asthma to the Asthma and Allergy Clinic of Azad University Hospitals (Farhihkhtegan, Amir-al-momenin and Bu-Ali, Tehran, Iran) in a period of one year (from October 2018 to October 2019) were enrolled in this cross-sectional study. All the parents were asked to fill a researcher-made questionnaire consisting of eight items regarding demographic information, family history of allergy, any type of allergies in the study population, and, specifically, the presence of a history of physician-diagnosed food allergy in early life.

2-2. Methods

After confirming the diagnosis of asthma and assessing its severity by a pediatric allergy specialist according to Expert Panel Report 3 (EPR3) (12) and Global Initiative for Asthma Management (GINA) (13), the patients' caregivers were asked to fill the questionnaire on the previous occurrence of a physician-diagnosed food allergy in their children.

2-3. Measuring tools

The severity of asthma was determined by the following definitions according to the Expert Panel Report 3 (EPR3) (12) and Global Initiative for Asthma Management (GINA) (13):

- Mild asthma: Asthma symptoms more than twice a week but not daily (12, 13);
- Moderate asthma: Daily asthma symptoms or nighttime waking with asthma once a week or more (12, 13); and
- Severe asthma: Asthma symptoms throughout the day or nighttime waking with asthma once a week or more, and poor lung function (12, 13).

2-4. Inclusion and Exclusion Criteria

2-4-1. Inclusion criteria

An age range of one to 14 years, having signs or symptoms of asthma, a previous history of physician-diagnosed food allergy, and the willingness of the patient to participate in the study were the inclusion criteria of the study.

2-4-2. Exclusion criteria

The presence of diseases other than food allergy that could influence the risk of poor asthma control, such as allergic rhinitis, gastroesophageal reflux, and rhinosinusitis as comorbid factors, and exposure to secondhand cigarette smoke were the exclusion criteria. The patients could quit the study whenever they decided.

2-5. Ethical consideration

This study was carried out following the recommendations of the Ethics Committee of Islamic Azad University of Medical Sciences. Written informed consent was obtained from all of the parents. The Ethics Committee of Islamic Azad University of Medical Sciences (reference number IR.IAU.TMU.REC.1397.356) approved the study protocol.

2-6. Data analysis

The collected data were analyzed using IBM SPSS for Windows, Version 22 (IBM Corp., Armonk, NY, USA). Descriptive statistics such as percentages and frequency distributions of different characteristics were used as appropriate. The Chi-square test was used to compare the categorical variables. The statistical significance level was set to $p<0.05$ for all association analyses.

3- RESULTS

A total of 170 asthmatic patients with different levels of asthma severity were enrolled in the study. The mean age of the patients was 7.1±3 years (with one-year old and 14-year-old as the youngest and the oldest participant, respectively). Ninety-two (54.1%) of the patients were males and the remaining were females (45.9%). **Figure.1** demonstrates a summary of recruitment of the patients in this study. Forty-two of the patients had a positive family history of allergic disorders.

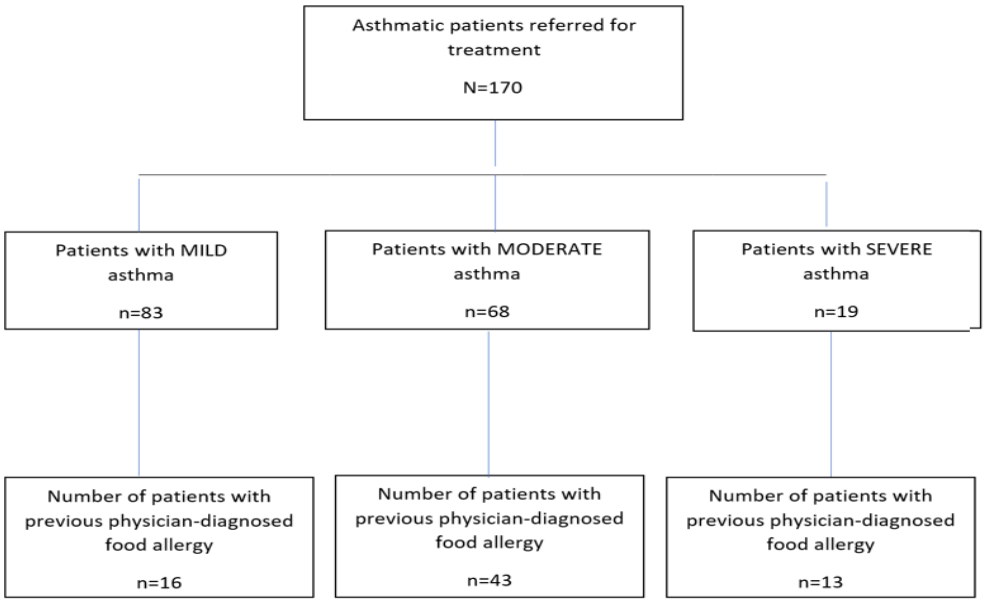

Fig.1: Recruitment and participant flow through the study based on consort diagram. One hundred seventy patients with childhood asthma were identified. The patients were categorized in three subgroups of mild, moderate and severe asthma. The number of patients with history of previous physician-diagnosed food allergy was sought in each of the subgroups.

Table.1 demonstrates the significant relationship between positive family history and food allergy in these patients. At the time of the first evaluation, the patients were categorized into three main groups of mild (83 patients), moderate (68 patients), and severe asthma (19 patients) according to EPR3 and GINA. Next, the frequency of self-reported food allergy was evaluated in each of these groups.

Table-1: Frequency of food allergy in patients with positive family history.

Food Allergy	Family History Number (%)		Total asthmatic patients Number (%)
	Yes	No	
Yes	28 (66.7)	44 (34.4)	72 (42.4)
No	14 (33.3)	84 (65.6)	98 (57.6)
Total	42 (100)	128 (100)	170 (100)

Table 2 displays the frequency of food allergy in the three groups of severity in the studied population. **Table 3** shows a comparison of p-value of the co-existence of previous food allergy history with asthma according to different levels of asthma severity. As shown, statistical analysis reveals a significant relationship between food allergy and asthma ($p<0.001$). Comparing data in different groups of severity revealed a significant relationship based on a history of food allergy in children with moderate and severe asthma compared to those with mild asthma ($p<0.001$). However, a meaningful relationship was not found when comparing moderate and severe asthma ($p=0.6$).

Table-2: The frequency of food allergy in different levels of asthma severity

Groups	Frequency	%
Mild Asthma		
Food Allergy positive	16	19.3
Food Allergy negative	67	80.7
Total	83	100
Moderate Asthma		
Food Allergy positive	43	63.2
Food Allergy negative	25	36.8
Total	68	100
Severe Asthma		
Food Allergy positive	13	68.4
Food Allergy negative	6	31.6
Total	19	100

Table-3: A summary of p values comparing the occurrence of food allergy in three groups of asthma severity.

Severity Comparison	P-value
Mild versus moderate asthma	< 0.001
Mild versus severe asthma	< 0.001
Moderate versus severe asthma	= 0.6

4- DISCUSSION

Considering the strong association between food allergy and asthma, the coexistence of the two conditions may increase the risk of severe episodes of asthma (14). Therefore, it is necessary to investigate the consequences of these two conditions and their mutual influence. In this study, we evaluated the asthmatic patients to find out whether they had a previous physician-diagnosed food allergy

and, if positive, its relationship with the severity of asthma later in life. The concept of "allergic march" has been suggested to explain the interrelationships among allergic diseases (15). Allergic march has been well known for years and indicates a temporal progression of allergic disorders (15). Food allergy appears early in the progression of atopic march (16), and it has been estimated that food allergy may trigger bronchial obstruction in 2-8.5% of children with asthma (17). Reports suggest that food allergy may increase the severity of asthma later in life. Friedlander surveyed 300 asthmatic children, 24% of them with food allergies, and showed an increased risk of hospitalization for their asthma (18). Vogel showed that food allergy was an independent risk factor for ICU admission in a pediatric population of 72 patients (19). Sherenian et al. have reported poorer results of lung function test in patients with two or more types of food allergy (16). As shown, all of the abovementioned studies point to a relationship between previous history of food allergy and the level of severity of asthma later in life. Although the precise underlying mechanism has not been understood, it has been proposed that a Th2 inflammation may arise as a result of food allergy, which leads to asthmatic phenotype later in life (20). Food allergy is a well-known risk factor for developing asthma but not is not a direct trigger of food-induced asthmatic reactions. Food allergic reactions may increase nonspecific bronchial hyper-responsiveness (21). In this study, most of the children with mild asthma had a history of transient wheezing with viral respiratory infections, and a positive family history of allergic disorders was detected in 9.6% of the cases. A significant relationship was found between food allergy in infancy and the later development of moderate to severe asthma in childhood and adolescence. The results of the present study also indicate that a history of food allergy may play a role as a relevant risk factor in determining the severity of asthma in the future. It is not implied that food allergens directly trigger an asthma attack in asthmatic children. Rather, the emphasis is on the role of previous food allergy and its resultant cumulative inflammation on later development of poorly controlled asthma. These factors make asthma a persistent condition despite no direct causal relationship between food ingestion and asthma exacerbation. The present study has faced some limitations. The first is that the study design was cross-sectional, while longitudinal cohort studies are more reliable in this regard. The second limitation is that this study relies on the information provided by the patients' caregivers, which may include biases such as recall bias or bias due to the educational level of parents completing the questionnaire.

5- CONCLUSION

The findings of this study conclude that food allergy in childhood is the distinguishing point between persistent wheezing from the transient form (e.g. as a result of viral infections). This factor, in addition to positive family history, provide clinical clues to predict higher levels of severity and worse outcomes. Therefore, food allergy together with a positive family history are suggested as risk factors for persistent problematic asthma, which places patients at greater risk of morbidity. A history of previous food allergy in infancy had a significant association with higher levels of asthma severity later in childhood.

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7- CONFLICT OF INTEREST: None.

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