Prevalence of food allergy in asthmatic patients

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ABSTRACT

Objectives: This study was conducted to assess the role of clinical sensitivity to food on the pattern of bronchial asthma.

Methods: A total of 1341 patients with asthma were included in the present study. The clinical sensitivity to food and its relation to respiratory symptoms were assessed cross-sectionally (using detailed questionnaires), and longitudinally during their regular visits to the asthma clinic using diet diary. Total IgE was determined for a subsample of the patients (No = 392).

Results: The prevalence of clinical sensitivity to food was 29%; about 2 thirds of the patients had high total IgE level. Asthmatic patients with clinical sensitivity to food present with some particular features which are considered risk factors that determine the occurrence and clinical pattern of asthma. In addition, some personal characteristics in the asthmatic patients make them at increased risk to have clinical sensitivity to food.

Conclusion: From the clinical experience of asthma management in our clinic, the authors believe and emphasize that elimination of food items from the diet of an asthmatic patient should be considered after careful investigation and observation of the patient. In addition, some personal characteristics in the asthmatic patients make them at increased risk to have clinical sensitivity to food. Early detection of food allergy is an important preventive factor for food related respiratory symptoms. The natural course of food allergy is of resolution over time although this may differ between foodstuffs and may be variably affected by avoidance of the offending allergen.

Keywords: Bronchial asthma, clinical sensitivity to food, principle component analysis, food allergy.

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Bronchial asthma is characterized by chronic coughing, phlegm production, shorting of breath, and wheezing. The estimated cumulative prevalence rates range from 2.8% to 7.23%.[1,2] Several studies have revealed that certain risk factors are associated with increased incidence of bronchial asthma, such as age, smoking habits, and occupational exposure.[3-5] Food allergy is now accepted as one of the causes of atopic dermatitis[6,7] acute urticaria,[8-10] reaction of the alimentary tract, and of acute systemic anaphylaxis.[11,12] The role of dietary factors in the development and course of asthma appears to be less clear.[13-20] Some investigators[21,22] estimate that it is a frequent cause of asthma in children or adults, whereas other investigators believe it is unimportant.[23,24] Some specific food allergies have received particular prominence. Peanut allergy is estimated to occur in 1.3% of children by age 4, asthma being a common manifestation, and it has been suggested that this allergy is now developing at younger ages.[25] Fish allergy has been described in 4.5% of 558 children referred for atopic disease[26] and the incidence of cows' milk allergy has been variously estimated between 1.8 and 7.5%.[27] To evaluate the effects of dietary factors on the development of asthma, we investigated the

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association between clinical sensitivity to different food items and daily variation of asthma symptoms, pattern of attacks, progression of the disease and age of onset of asthma.

Methods. The present study included all patients with asthma who attended the asthma follow-up clinic at King Abdulaziz University Hospital during three year-period (number = 1341 patients).

The diagnosis of bronchial asthma and the protocol followed in the asthma clinic was reported else where by El-Gamal et al, 1993.[28] Each patient was asked a detailed questionnaires about personal characteristics, respiratory symptoms and smoking habits using the Medical Research Council (MRC) questionnaire;[29] and questions about the allergic state, age of onset of asthma, provoking agents and family history of asthma. Detailed inquiry about relation between consumption of a number of allergenic food stuff (available in the region) and occurrence of clinical sensitivity was also included in this questionnaire. Only those who were certain about positive clinical sensitivity to a particular type(s) of food were given score 1. If the patient gave a negative clinical history of food allergy, or was not certain about the association, a 0 score was given. These responses, were confirmed during the follow up visits of the patients to the asthma clinic (using special dietary diary).

Total IgE concentrations were determined by Phadebase IgE PRIST^{R} (Pharmacia Diagnostics, Uppsala) according to the recommendations of the manufacturer using serum dilution of 1/5.

The SPSS/PC+, statistical routines were used for the analysis of the data.[30] The data were subjected to principle component regression technique where the following steps were performed[31-33] the original data were standardized (centered and scaled); a cross correlation matrix between the variables was prepared; factors were extracted using the principal-component solution without interaction. In this method the main diagonal of the correlation matrix is not altered, and the program extracted principal components which are defined as exact mathematical transformation of the original variables. A variable can be decomposed into components and predicted exactly from these components; the extracted components were rotated using "varimax" type of rotation to obtain orthogonal factors with simple structures; and logistic and least square multiple regressions were performed on the extracted components using step-wise regression technique. The categorical variables were coded as dummy variables (1,0), and were used in the models as outcome or predictor variables. The results were considered significant if the p-value was less than 0.05.

Results. Perception of clinical sensitivity to food was reported by 29% of the patients with asthma (392 patients). These patients had multiple food hyper-sensitivity (Table 1). Sensitivity to food was significantly reported more among those over 15 years of age (85%) compared to those in the young age group, (15.3%), where p was <0.05. Allergy to food was higher in women, 30% than men, 28%, however p was >0.05. Proportions of patients with clinical sensitivity to food was greater in patients with positive family history of allergy (55%) compared to those with no family history of allergy (45%), the p value was <0.05. Over 90% of patients with food allergy were encountered in patients who had other allergic disorders (atopic patients), compared to those who did not (8%). Total IgE level was elevated in 64.5% of the patients with clinical sensitivity to food allergy.

The relationships between obtained orthogonal factors and the variables which had significant loading on them are displayed in Table 2. Factor 1 was mainly identified with age of onset of asthma and age of the patient (r = 0.98 and 0.72 respectively). Factor 2 was identified mainly with variable duration of asthma (r = 0.99); while factor 13 was identified mainly with the variable smoking (r = 0.99). Each one of the rest of the factors was identified with only one food item.

Clinical sensitivity to citrus fruits (factor 15) was significantly associated with increased risk of asthmatic attacks at night compared to those who did not have allergy to citrus fruits. Clinical sensitivity to

Table 1 - Some of the most common food allergens suspected in asthmatic patients with clinical sensitivity to food (Number = 392).

Suspected food	No. of subjects (%)
Egg	312 (80)
Banana	264 (67)
Fish	233 (59)
Tomatoe	136 (35)
Cirtus fruits	132 (34)
Strawberry	124 (32)
Nuts	80 (20)
Cow's milk	68 (17)
Beer	52 (13)
Melon	48 (12)
Mushroom	36 (9)

Table 2 - Varimax rotated factor matrix* showing relationship between rotated factors and different variables.

Variables	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12	F13	F14	F15	F16	F17
Age of onset	.98																
Age	.72																
Duration of asthma	-	.99															
Egg	-	-	.87														
Beer	-	-	-	.89													
Cow's milk	-	-	-	-	.94	.											
Tomatoes	-	-	-	-	-	.85											
Strawberry	-	-	-	-	-	-	.87										
Banana	-	-	-	-	-	-	-	.84									
One's history of allergy melon	-	-	-	-	-	-	-	-	.98								
Melon	-	-	-	-	-	-	-	-	-	.84							
Sex	-	-	-	-	-	-	-	-	-	-	.99						
Family history of asthma	-	-	-	-	-	-	-	-	-	-	-	.98					
Smoking	-	-	-	-	-	-	-	-	-	-	-	-	.99				
Mushroom	-	-	-	-	-	-	-	-	-	-	-	-	-	.84			
Citrus fruits	-	-	-	-	-	-	-	-	-	-	-	-	-	-	.81		
Fish	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	.77	
Nuts	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	.75

*Variables which had loading greater than 0.5 were identified with the factors

Table 3 - Logestic regression relationships between factor scores and variables: daily variation, seasonally progression and age of onset of asthma.

Dependent variables			
Daily variation (day=0, Night=1) **Factor Score B (expB)**	**Seasonally (perineal=1, seasonal=0)** **Factor Score B (exp B)**	**Progression (progressive=1, regressive=0)** **Factor Score B (exp B)**	**Age of onset (<15yrs=1, ≥15 yrs=0)**
F1 -0.63 (0.53)*	NS	0.34 (1.40)*	-0.24 (0.79)*
F2 -0.21 (0.81)*	NS	-0.14 (0.86)*	NS
F3 NS	NS	0.34 (1.40)*	NS
F4 NS	NS	0.35 (1.43)*	NS
F5 NS	NS	NS	0.12 (1.12)*
F6 NS	-0.41 (0.67)*	NS	NS
F7 NS	NS	NS	NS
F8 NS	NS	NS	NS
F9 NS	0.85 (2.34)*	0.63 (1.87)*	NS
F10 NS	NS	0.86 (1.15)	NS
F11 NS	-0.58 (0.56)*	NS	-0.20 (0.81)
F12 -0.22 (0.81)*	NS	0.14 (2.37)*	NS
F13 NS	-12.81 (0.00)*	NS	NS
F14 NS	NS	NS	NS
F15 0.33 (1.39)*	NS	0.37 (1.45)*	NS
F16 NS	NS	0.22 (1.24)*	NS
F17 NS	NS	NS	
Constant 2.292	-4.37	0.63	0.07

*p-value <0.05

Table 4 - Logistic regression relationships between factor scores and variables: positive allergic response to food items.

		Predictor variables					
Dependent variables		**F1 B (exp B)**	**F2 B (exp B)**	**F9 B (exp B)**	**F11 B (exp B)**	**F12 B (exp B)**	**F13 B (exp B)**
Cow's milk	-3.01	0.02 (1.02)	0.24* (1.27)	0.27 (1.31)	-0.20 (0.82)	0.05 (1.05)	-0.15 (0.87)
Mushroom	-3.72	0.08 (1.08)	0.17 (1.18)	0.19 (1.20)	-0.45* (0.64)	0.13 (1.13)	-0.09 (0.92)
Egg	-1.22	0.14 (1.15)	0.09 (1.10)	0.27* (1.31)	-0.01 (0.99)	0.04 (1.04)	0.01 (1.01)
Tomatoes	-2.23	0.29* (1.34)	0.03 (1.03)	0.12 (1.13)	-0.03* (0.97)	0.13 (1.14)	0.08 (1.09)
Fish	-1.59	0.13 (1.14)	0.06 (1.06)	0.21* (1.23)	0.07 (1.06)	0.06 (1.06)	-0.01 (0.99)
Strawberry	-2.33	0.14 (1.15)	0.25* (1.28)	0.17 (1.19)	-0.04 (0.96)	0.10 (1.10)	-0.02 (1.00)
Banana	-1.43	0.20* (1.22)	0.09 (1.09)	0.13 (1.14)	0.07 (1.06)	0.01 (1.01)	-0.04 (0.96)
Citrus fruits	-2.31	0.32* (1.37)	-0.01 (0.99)	0.26* (1.29)	0.09 (1.10)	0.26* (1.30)	-0.10 (1.10)
Melon	-3.40	0.29 (1.35)	-0.09 (0.91)	0.25 (1.29)	-0.25 (0.78)	0.02 (1.02)	-0.14 (0.87)
Hazel Nuts	-2.82	0.16 (1.17)	0.12 (1.13)	0.04 (1.04)	-0.22 (0.81)	0.06 (1.06)	-0.25 (0.78)

*p-value <0.05

Table 5 - Regression relationship between IgE percent of normal and different factor scores.

IgE level (percent of normal) Dependent variable				
Predictor variables	**B**	**SE B**	**t-test**	**p-value**
F1	17.79	13.83	1.28	0.199
F2	-16.27	15.34	-0.04	0.289
F3	-02.98	13.48	-0.22	0.825
F4	05.22	33.42	0.15	0.876
F5	-44.36	27.41	-1.62	0.106
F6	50.21	17.61	2.85	0.004
F7	-79.47	22.64	-3.51	0.000
F8	-24.77	16.84	-1.47	0.141
F9	41.15	12.59	3.26	0.001
F10	55.82	22.88	2.44	0.015
F11	59.89	13.69	4.37	0.000
F12	10.64	13.55	0.78	0.432
F13	03.43	17.01	0.20	0.840
F14	-36.22	21.96	-1.64	0.099
F15	90.47	22.77	3.97	0.000
F16	-13.76	15.18	-0.91	0.365
F17	-28.32	15.96	-1.77	0.076

tomatoes (factor 6) was significantly associated with seasonal fluctuation in asthmatic attacks. Positive history of allergy to egg (factor 3), beer (factor 4), melon (factor 10), citrus fruits (factor 15) and to fish (factor 16) are associated with increased severity and frequency of asthmatic attacks. Clinical sensitivity to tomatoes (factor 6) was associated with increased risk of having asthmatic attacks before the age of 15 years (Table 3).

Increased age of onset of asthma, and age of asthmatic patients were significantly associated with increased reporting of clinical sensitivity for tomatoes, banana, and citrus fruits. Increased duration of asthma was significantly associated with increased risk of developing clinical sensitivity to cows' milk and strawberry. Personal history of allergy was a significant risk factor for having clinical sensitivity to egg, fish and citrus fruits. Females are at greater risk of having food allergy to mushroom compared to males. Positive family history of asthma was a significant risk factor for clinical sensitivity to citrus fruits. Smoking was not significant predisposing risk factor for having clinical sensitivity to studied types of foods (Table 4).

Table 5 depicts the regression model which describes factors affecting IgE level. Positive history of allergy to tomatoes (factor 6), mellon (factor 10) and citrus fruits (factor 15) were significantly associated with increased level of IgE in the blood of the asthmatic patients. On the other hand, positive history of allergy to strawberry was significantly associated with decreased level of IgE.

Discussion. The main objective of the present study was to assess the relationship between perceived clinical sensitivity to food and clinical aspects of bronchial asthma (e.g; pattern and course of asthmatic symptoms). Clinical studies have demonstrated the reduced reliability to patient history, skin tests, RAST, and various other methods in accurately predicting the presence of food allergy, compared with double-blind placebo-controlled food challenge (DBPCFC). Only a fraction of patients who have skin allergy and circulating IgE antibodies to foods develop symptoms when they are challenged with the offending food.[34-36] In the present study, great care was taken to confirm the clinical sensitivity to food, as patients attended the asthma clinic were interviewed by a specialist doctors (the two authors), who spent at least 20 minutes with each patients as a part of the protocol developed and implemented in the clinic to treat patients with asthma.[28] Specific foods were suspected as causative when the asthmatic symptoms (e.g; wheeze, cough, and shortness of breath) were clearly related to food ingestion and when striking improvement followed food elimination. Large proportion of patients, on their first visit to the asthma clinic at KAUH, used to have some common food items known to be allergenic (eg. fish, milk, egg, banana, and strawberry) eliminated from their diets based on the advice of their treating doctors, or based on general knowledge from relatives or friends without proper establishment of relationship to their asthmatic symptoms. These patients were discouraged to do that, and were followed up in the clinic on monthly basis and a specific diary was used to describe the dietary history before any worsening of the symptoms. Patients who were in doubt, or denied such a relationship were considered as non-sensitive to food. Thus the possibility of misclassification bias in the prevalence of clinical sensitivity to food among our asthmatic patients was minimized to a reasonable extent.

The results of the present study indicate a prevalence of 29% for self reported food allergy, the prevalence being higher in women (30%) than men (28%). Similar prevalence, and comparable differences between women 26% and men 19% were found by Burr and Merrett[37] and also by Bender and Mettews[38] (39% and 26%). Young et al,[39] and Jansen et al[40] reported lower prevalence. This large variation in prevalence figures can be explained by the subjective nature of the relationship between complaints and food consumption, the varying ways in which the survey questions were formulated and the ways responses were obtained.

Several studies revealed that egg and fish were the most frequent offending antigens responsible for positive DBPCFC among patients.[10,22] The present study confirmed these findings, where egg was the most frequent food incriminated in clinical hypersensitivity among our patients, followed by banana and fish.

This is a difficult and time consuming procedure requiring a run-in period, during which the subject omits the possible offending item from the diet, followed by a challenge in which foodstuffs are presented in tablet or powder form with appropriate placebo controls. There have been no studies where this complex technique has been used on large population samples. More often, subjects have been asked by questionnaire to report a possible food allergy or intolerance and the result is that prevalence figures in the literature are estimates. In contrast to general population surveys, an alternative approach has been to study selected populations. Novembre et al investigated 140 children with asthma using a clinical history, RAST testing and double blind food challenges and found that 9% had food related respiratory symptoms, 6% having asthmatic reactions.[42] James and colleagues studied 320 children with atopic dermatitis using DBPCFC.[43] This group of children was highly atopic and food hypersensitivity was confirmed by challenge in 64% of the subjects, 17% describing expiratory wheezing. Thus within these selected populations, a much

higher prevalence of reactions to foodstuffs was detected.

In the present study perception of clinical sensitivity to food was reported by 29% of the patients with asthma (392 patients). Earlier studies revealed that large number of patients with asthma who had suspected food allergy had high serum IgE levels including high RAST titer to tested food, and positive DBPCFC.[22,41] In the present study also about two thirds of the patients (64.5%) with perceived clinical sensitivity to food had high total serum IgE level; this was particularly significant in patients who gave clinical sensitivity to tomatoes, melon, and citrus fruits. In the present study, some patients with asthma (35.5%) reporting clinical sensitivity to food had normal total IgE concentration. This is consistent with other studies[22,41] which failed to demonstrate neither increased mean serum IgE concentration, nor detectable amount of IgE antibodies to the tested food to patients with suspected food allergy. The symptoms of these patients were probably based on other immunological or non-immunological mechanisms.[44,45]

The present study revealed that, after allowing for the various confounding factors, patients with asthma who are allergic to food present some particular features. Those who reported clinical sensitivity to egg, melon, citrus fruits and fish were significantly at more risk to have severe form of asthma. Reporting clinical sensitivity to tomatoes was significantly associated with young onset and episodic type of asthma, while sensitivity to citrus fruits was associated with increased risk of night attacks of asthma.

The present study revealed that some personal factors were found to be significant determinants of clinical sensitivity to food. Most patients who reported food allergy were adults, with late onset asthma. This is similar to other studies.[11-14] Increased duration of asthma was a determinant risk factor for reporting clinical sensitivity to cow's milk and strawberry. In agreement with other studies,[22,41] the present study revealed that asthmatic patients with either allergic rhinitis, and atopic dermatitis or both were at increased risk to suffer from clinical sensitivity to food particularly egg, fish and citrus fruits. Positive family history to asthma, had a similar risk particularly to citrus fruits. Smoking demonstrated no effect on the perception of clinical sensitivity to food in our patients. Early identification of symptomatic food allergy at young age and then avoiding it, is an important preventive factor for food allergy resolution overtime. Sampson and Scanlon have shown a 26% loss of symptomatic food allergy to five major allergens (egg, milk, soy, wheat and peanut) and a 66% loss to other food allergens in patients adhering to elimination diets,[46] which appears to differ between foods.[47]

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