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Food Allergy as a Risk Factor for Asthma Morbidity in Adults

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Background. The objective of this study was to evaluate the relationship between food allergy and asthma morbidity in adults. **Methods.** We interviewed a cohort of persistent asthmatics from an inner-city clinic. Allergies to food were assessed by patient report of convincing symptoms of acute allergic reactions. Outcome variables included health resource utilization and medication use. **Results.** The prevalence of allergy to fish, peanut, tree-nut, shellfish, and seed allergies were 3%, 3%, 3%, 13%, and 1%. Patients with allergies to >1 food had increased asthma hospitalizations, ED visits, and use of oral steroids ($p < 0.05$ for all comparisons). Specifically, allergy to fish was associated with a greater risk of health resource utilization and increased frequency of oral steroid use ($p \leq 0.03$ for all comparisons). **Conclusions.** Self-reported allergy to foods was associated with worse outcomes, suggesting that food allergy may be a risk factor for increased asthma morbidity in adults.

Keywords asthma, food allergy, morbidity, outcomes, risk factors

INTRODUCTION

Asthma is a highly prevalent disease, affecting over 5–10% of the United States (US) population. Morbidity from asthma has been increasing in the United States in the last several years, particularly in urban areas (1). Reducing asthma morbidity is a key focus of numerous payer, provider, and public health initiatives (1, 2). A better understanding of the underlying mechanisms and risk factors for poor asthma control is therefore essential to improve the outcomes of these patients.

Several risk factors for increased asthma morbidity have been identified in the literature (3–10). Among the most commonly reported factors are demographic, socioeconomic, clinical, psychosocial, and environmental variables. The association of asthma morbidity and allergy has also long been recognized. Sensitization and exposure to indoor allergens play a key role in difficult-to-control asthma (7, 11–13). Studies have shown a correlation between positive skin tests for allergens (14) as well as elevated serum IgE levels with not only asthma prevalence but asthma severity (15, 16). Moreover, higher exposure to allergens is one of the proposed explanations for the increased asthma morbidity among inner-city residents (17, 18).

A number of studies also have examined the extent to which food allergies are related to asthma (19–23). Food allergies also are common in the United States, with about 6% of

children and 4% of adults suffering from some type of allergy (24). There is evidence of higher asthma prevalence among individuals with food allergy, especially those with life-threatening hypersensitivity (22, 25). Only a few studies, however, have reported a potential link between asthma morbidity and food allergy, most of which have been limited to children (27–29). Thus, it is unknown whether food allergies are associated with increased morbidity in adult asthmatics. In this study, we assessed the prevalence of self-reported food allergies among a cohort of adults with asthma to evaluate whether they are associated with poor asthma control and worse outcomes.

METHODS

This cross-sectional study included a cohort of adults with asthma recruited from the general medicine clinic of Mount Sinai Hospital, situated in East Harlem, New York City. Data were collected over a 15-month period, from June 2004 to August 2005. Potentially eligible patients were identified by screening the clinic's registration system for all adults with a physician diagnosis of asthma. Patients were eligible if they were ≥ 18 years of age and spoke English or Spanish. To ensure a patient population with sufficient symptoms and severity to allow identification of related risk factors, we limited our study to patients of with mild persistent, moderate persistent or severe asthma, defined according to the National Heart, Lung and Blood Institute's Expert Panel on Asthma (30). Individuals with a smoking history of ≥ 10 pack-years, a diagnosis of chronic obstructive lung disease, or other chronic respiratory illness were excluded from the study. Mount Sinai's Institutional Review Board approved the study.

Trained research staff conducted an interviewer-administered survey in English or Spanish. We collected information on sociodemographics, access to care data, asthma medications and comorbidities. History of food

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allergy was determined based on self-reported data using published criteria (31). The food allergy items included detailed questions about history of allergic reactions to fish, peanuts, tree nuts, shellfish, seeds, milk, and eggs including comprehensive descriptions of the type of foods belonging to each group. Additional questions were administered to individuals reporting allergic reactions, including the type of reaction, associated symptoms, timing of symptoms in relation to food ingestion, symptom recurrence following repeated exposure, and whether the patient was able to continue consuming the specific food.

Hives, angioedema, difficulty breathing, oral pruritus, and throat closing were considered as convincing symptoms of allergy if they occurred within 1 hour of food ingestion. Light-headedness and coughing were considered convincing symptoms only if they were reported in combination with a supportive symptom such as nausea, abdominal pain, vomiting, or diarrhea. Using this information, patients were categorized on as being allergic if they reported having ≥ 1 convincing symptom within 1 hour of ingestion of a specific food.

We also collected data regarding history of physician diagnosis of sensitization to aeroallergens (cats, dogs, birds/feathers, dust mites, cockroaches, molds, and grasses) and type of test used (skin prick testing vs blood testing). Patients with sensitization to 2 or more allergens were classified as atopic.

We used several established measures of asthma morbidity. These included history of hospitalizations for asthma, Emergency Department (ED) visits, prior intubation, and oral steroid use. Patients were asked whether they were ever hospitalized or intubated (including the number of times) due to asthma during their lifetime. Additionally, subjects were asked about the number of asthma hospitalizations, ED visits, and courses of oral steroid in the year prior to enrollment.

Statistical Analysis

We used the Fisher Exact test to examine the association between food allergy and history of asthma hospitalization and ED visits. Differences in number of lifetime intubations and the frequency of oral steroid use during the year prior to enrollment were assessed using the Mann-Whitney test. Multiple logistic regression was used to assess whether having >1 food allergy was associated with increased risk of hospitalization and ED visits after controlling for age, sex, race/ethnicity, socioeconomic status, and atopy (sensitization to ≥ 2 aeroallergens). Similarly, linear regression models were used to test if patients with >1 food allergy had increased number of intubations or oral steroid use after controlling for potential confounders. These models were built manually using a forward strategy. Variable testing was performed using the likelihood ratio test.

Given the low rates of allergy to specific foods in adults, we could not use formal multivariate analysis to control for other established risk factors for asthma morbidity in the comparisons involving allergy to individual foods. In order to test for potential confounding however, we assessed the correlation between allergy to specific foods and asthma morbidity risk factors using the Spearman's rank correlation coefficient. Lack of correlation between food allergy and other risk factors would suggest that these variables are not likely

TABLE 1.—Demographic and clinical characteristics of study patients, $N = 203$.

Characteristic	Value
Age (yrs), mean $\pm$ SD	48 $\pm$ 13
Female (%)	86
Hispanic Ethnicity (%)	60
Insurance Status (%)	
Medicaid	66
No Insurance Over Past Year (%)	11
Native Language (%)	
Spanish	35
Income $<$ \$15,000 (%)	68
Education $<$ High School (%)	39
Asthma Severity (%)	57
Lifetime Hospitalizations	
≥ 1 Intubation over Lifetime	11
Past Year Emergency Department Visits	52
Past Year Hospitalizations	23
≥ 1 Oral Steroid Use in Past Year	48
Asthma Regimen (%)	
Inhaled Corticosteroid or Leukotriene Inhibitor	87
Short acting beta-2 agonist alone	13
Prevalence of Physician Diagnosis of	
Allergies to Aeroallergens (%)	
Dust Mites	47
Cat	32
Cockroaches	31

confounders of the observed unadjusted association in our cohort. All analyses used 2-tailed significance levels of 0.05 and were conducted with SPSS statistical software (SPSS Inc., Chicago, IL).

RESULTS

Between June 2004 and August 2005, 784 patients with a probably history of asthma were identified from the computerized registration system and assessed for study eligibility. Of these, 567 were excluded due to: no history of physician diagnosis of asthma (151 patients), mild intermittent asthma severity (146 patients), history of smoking >10 pack-years (103 patients), other chronic lung disease (69 patients), cognitive impairment (25 patients), and other reasons (73 patients). Of the remaining 217 eligible patients, 14 (7%), declined study participation, leaving a cohort of 203 adult patients with asthma.

The baseline characteristics of the cohort are shown in Table 1. Consistent with the epidemiology of inner-city asthma, this was largely a group of low-income, predominantly Hispanic and African American women (9, 11). The mean age of patients was 48 ± 13 years and 86% were female. Sixty-eight percent of patients had an annual income below \$15,000.

Fifteen percent of patients reported convincing symptoms of allergy to one food and 7% reported allergies to more than one food (Table 2). The most prevalent food allergy was shellfish with 13% of patients reporting convincing symptoms within 1 hour after ingestion. Other food allergies were reported less frequently: fish (3%), peanut (3%), tree nut (3%), seeds (1%), milk (1%), and eggs (1%).

Association Between Food Allergy and Asthma Morbidity

Patients with convincing symptoms of >1 food allergy were more likely to have ever been hospitalized for asthma, had increased number of ED visits in the past year, and higher number of oral steroid courses during the year prior to enrollment ($p < 0.05$ for all comparisons; Table 3). Data regarding

TABLE 2.—Prevalence of food allergy among study participants, $N = 203$.

Type of food allergy	Prevalence of food allergy (%)
Number of Food Allergies	
0	78
1	15
≥ 2	7
Specific Foods	
Shellfish	13
Peanut	3
Tree Nut	3
Fish	3
Milk	1
Eggs	1
Seeds	1

the presence of convincing symptoms following ingestion of different foods showed that the association with asthma morbidity was stronger among some specific food types. Fish allergy was associated with increased risk of lifetime hospitalizations, past year ED visits, past year hospitalizations, and increased frequency of oral steroid use during the last year ($p < 0.05$ for all comparisons). Having convincing symptoms of peanut allergy was associated with increased number of intubations ($p = 0.03$) and borderline associated to lifetime hospitalizations ($p = 0.07$). Shellfish allergy was associated with increased frequency in oral steroid use during the past year ($p = 0.03$). Seed allergies were associated with an increase in past year hospitalizations as well as increased frequency in oral steroid use ($p < 0.05$ for all comparisons). In contrast, allergies to milk and egg were not associated with any of the asthma morbidity outcomes evaluated (data not shown).

Analyses Adjusted for Other Risk Factors for Asthma Morbidity

Multivariate analyses showed that allergy to > 1 food was independently associated with higher risk of lifetime hospitalizations and ED visits for asthma, and to increased frequency of oral steroid use even after adjusting for other risk factors (Table 4). Table 5 shows the correlation between presence allergy to specific foods and other established risk fac-

tors for worse asthma outcomes. Overall, the presence of food allergy was not correlated to sociodemographic characteristics, comorbidities, or sensitization to aeroallergens. Most of the correlation coefficients moreover, showed a negative association between these variables, providing further evidence against the possibility of confounding.

DISCUSSION

Food allergy has been reported as a risk factor for increased morbidity among children with asthma (27–29). In this study, we examined the association of food allergy with asthma morbidity in adults. Using data from 203 patients with persistent asthma, we found that convincing symptoms of food allergy were associated with several established measures of asthma morbidity, including risk of hospitalizations, ED visits, intubations, and oral steroid use. These data suggest that allergy to food might be linked to worse outcomes in adult asthmatics. Given the low prevalence of food allergy among adults in general, and in our cohort in particular, these findings should be confirmed in larger studies.

The relationship between sensitization to environmental allergens and asthma has been clearly established (7, 11–13). Few studies however, have evaluated the potential role of food allergies as a risk factor for increased asthma morbidity. A study including 19 children ventilated for an exacerbation of asthma and 38 matched controls found that food allergy was an independent risk factor for life-threatening asthma with an adjusted odds ratio of 5.9 (27). Similarly, in a cohort study of peanut-allergic children, 4 of the 46 subjects died of an exacerbation of asthma over the 14-year follow-up period, suggesting that peanut allergic children may have a greater risk of dying from asthma (32). The literature on adult asthmatics, however, has been limited to studies linking food allergy to increased asthma prevalence (25). Our findings extend the link between food allergy and asthma, suggesting that food allergy may be associated with increased asthma morbidity not only in children but in adults as well.

Although there is evidence of an association between food allergies and asthma, the pathophysiologic mechanism explaining this association is not well understood. Several

TABLE 3.—Association between food allergy and asthma morbidity.

Type of food allergy	Lifetime hospitalizations		No. ¹ of intubations over lifetime		Past year ED visits		Past year hospitalizations		No. of oral steroid use in past year	
	%	<i>P</i> value	Mean ² Difference	<i>p</i> value	%	<i>p</i> value	%	<i>p</i> value	Mean Difference	<i>p</i> value
> 1 Food Allergies	No	<0.01	0.40	0.14	50	0.05	22	0.10	1.89	<0.001
	Yes				79		43			
Peanut	No	0.07	0.39	0.03	51	0.37	23	0.33	1.34	0.14
	Yes				80		40			
Tree Nut	No	0.39	−0.12	0.43	51	0.06	23	0.99	1.66	0.08
	Yes				100		20			
Fish	No	0.04	0.22	0.61	50	0.03	21	<0.01	1.84	0.02
	Yes				100		83			
Shellfish	No	0.15	0.01	0.92	52	0.99	23	0.81	0.75	0.03
	Yes				52		26			
Seeds	No	0.51	−0.11	0.62	51	0.50	22	0.05	3.83	0.03
	Yes				100		100			

¹No. denotes number.²Shows the mean difference between the number of intubations for patients with and without the specific food allergy. Convincing symptoms to milk and egg allergies were not significantly associated to any of the measures of asthma morbidity.

TABLE 4.—Adjusted associated between allergy to >1 food and asthma morbidity.

Variable	Lifetime hospitalizations		No. ¹ of intubations over lifetime		Past year ED visits		Past year hospitalizations		No. of oral steroid use in past year	
	OR ²	p value ³	Parameter Estimate	p value ⁴	OR	p value ⁴	OR	pvalue ³	Parameter Estimate	p value ⁴
>1 Food Allergy	11.1	0.02	0.148	0.04	4.1	0.04	2.7	0.10	0.198	0.01

¹No. denotes number.
²OR denotes odds ratio.
³Analyses performed using logistic regression analysis.
⁴Based on the results of linear regression analyses.
All models were adjusted for age, sex, race/ethnicity, socioeconomic status, and presence of atopy.

studies have shown a link between food allergy or eosinophil-associated gastrointestinal diseases and increased bronchial hyperresponsiveness, even in non-asthmatics (19, 33, 34). It has been postulated that bronchial hyperresponsiveness in these conditions is a result of activation of immune cells (such as T lymphocytes) from the intestinal mucosa, leading to stimulation of the bronchial mucosa. Therefore, asthmatics who suffer from food allergy may have increased airway hyperreactivity and consequently may be more likely to experience worse morbidity. A second possible explanation is that food allergy may serve as a marker for a skewed host immune response, with a tendency to react with a pro-inflammatory allergic reaction.

Third, repeated accidental oral exposure to the offending foods or chronic inhalation of aerosolized food particles may result in continued cellular activation and production of pro-inflammatory cytokines that worsen asthma. Finally, recurrent respiratory symptoms or more severe anaphylactic reactions to food may have been misdiagnosed as asthma exacerbations in some of these individuals. Although most patients in our study with convincing symptoms of food allergy reported that they had eliminated the particular food from their diet, accidental ingestion of hidden sources of these food allergens remains a possibility.

Several limitations merit discussion. We identified patients allergic to food using self-reported data. The gold standard for diagnosing food allergy is the double-blind, placebo-controlled oral food challenge (35). However, this method is costly, carries risks, is time consuming and is rarely used in epidemiologic studies. Alternatively, skin tests may be used to identify sensitized patients; the accuracy of these tests for clinical allergy, however, is low (24). Studies using serum tests for food-specific IgE antibodies to predict clinical food allergy are promising but have only been performed in children (36, 37). Although we relied on self-reported

information, we limited our analysis to those with convincing symptoms of acute allergic reactions within an hour of ingesting the food. This approach has been used previously in epidemiologic studies and is based upon studies showing good accuracy (86–93%) compared to serologic and physician confirmed allergies (31, 38, 39). Additional studies using objective measures are needed however, to further assess the importance of food allergy as a cause of asthma morbidity among adults.

Due to the low prevalence of food allergy in the adult population, even among asthmatic patients, our study had limited power to detect weak associations between specific foods and asthma morbidity measures. Even so, we did find an independent relationship between food allergy and several asthma morbidity measures. Additionally, we could not perform formal multivariate tests to adjust for potential confounders for the analyses involving allergies to specific foods. We found however, low or negative correlations between other risk factors for increased asthma morbidity and specific food allergies, suggesting that these factors did not confound our results. Patients in the study were enrolled from a single inner-city clinic, hence the generalizability of the results is unknown. We deliberately studied an inner-city population because these patients have the highest rates of asthma morbidity in the country and the greatest need for interventions to improve their outcomes.

In our cohort, there was a consistent association between allergy to >1 food and most measures of asthma morbidity. The associations to specific foods however, were limited to certain outcomes. Additionally, not all food types were associated to worse asthma control. The low frequency of certain morbidity measures, such as prior intubations for asthma, may explain the observed pattern of associations. The accuracy of self-reported data may also vary for different foods, which may explain, in part, why our findings were limited to specific food types. Alternatively, some food types may be more likely to stimulate bronchial hypereactivity while others may be less so. This hypothesis is supported by prior studies showing that certain foods, such as fish, peanuts, and treenuts are more strongly associated with asthma prevalence than others (22, 28).

In summary, our findings suggest that food allergy might be a risk factor for increased asthma morbidity in adults. Further studies should validate these findings in large populations using objective measures of food allergy. If confirmed, these findings would have implications for the management of asthmatics, particularly those with severe disease.

TABLE 5.—Lack of association between presence of specific food allergies and other risk factors for asthma morbidity.

Risk factor	Food Allergy				
	Peanut	Tree Nut	Fish	Shellfish	Seeds
Male gender	0.02 ¹	0.12	0.01	−0.04	0.10
Age>55 years	−0.03	−0.10	0.01	0.13	−0.07
Hispanic	0.01	0.01	0.03	−0.06	−0.02
Income<\$15,000	−0.02	−0.02	−0.10	−0.16*	−0.06
Age of Onset<18 years	0.14	−0.01	−0.04	−0.04	−0.09
Atopy	0.06	−0.01	0.15*	0.06	−0.08

¹Spearman's correlation coefficient.
None of these associations were statistically significant except for *p ≤ 0.05.

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