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CLIN PEDIATR published online 17 May 2012

DOI: 10.1177/0009922812448526

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Clinical Pediatrics
XX(X) 1-6
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DOI: 10.1177/0009922812448526
http://cpj.sagepub.com


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Abstract

Objective. The aim of this study was to describe the distribution of childhood food allergy in the United States. **Methods.** A randomized survey was administered electronically from June 2009 to February 2010 to adults in US households with at least 1 child younger than 18 years. Data were analyzed as weighted proportions to estimate prevalence and severity of food allergy by geographic location. Multiple logistic regression models were constructed to estimate the association between geographic location and food allergy. **Results.** Data were analyzed for 38 465 children. Increasing population density corresponded with increasing prevalence, from 6.2% in rural areas (95% confidence interval [CI] = 5.6-6.8) to 9.8% in urban centers (95% CI = 8.6-11.0). Odds of food allergy were graded, with odds in urban versus rural areas highest (odds ratio [OR] = 1.7, 95% CI = 1.5-2.0), followed by metropolitan versus rural areas (OR = 1.4, 95% CI = 1.2-1.5), and so on. Significance remained after adjusting for race/ethnicity, gender, age, household income, and latitude. **Conclusions.** An association between urban/rural status and food allergy prevalence was observed.

Keywords

pediatrics, prevalence, urban, rural, vitamin D, epidemiology

Introduction

Food allergy is a serious and growing health problem, affecting 8.0% of children in the United States.¹ The prevalence rate has increased by at least 18% over the past decade.²⁻⁵ Furthermore, among affected children, nearly 40% have a history of severe reactions, ranging from a fall in blood pressure to an anaphylactic event.¹ Such data are particularly troubling, given the absence of a cure, limited treatment options, and the ubiquity of food in our society.

Several international studies have suggested that food allergy prevalence may vary at a regional level.⁶⁻⁹ Among the few studies conducted in the United States, regional differences have been extrapolated using data on epinephrine prescription history and visits to the emergency department¹⁰⁻¹² but have not been assessed using prevalence rates. Prevalence rates of comorbid atopic conditions, however, have been shown to vary by urban/rural status.¹³⁻¹⁷

A detailed analysis of food allergy distribution in the United States may provide insight into disease attributes and pathogenesis and may also highlight disparities in

care. Therefore, the objective of this study was to characterize the geographic distribution of food allergy prevalence in the United States using data from a nationally representative sample of nearly 40 000 children.

Methods

A population-based, cross-sectional survey was administered between June 2009 and February 2010 to a representative sample of US households with children. The institutional review boards of Children's Memorial Hospital and Northwestern University in Chicago,

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Illinois, approved the study protocol. Consent to participate was implicit on completion and return of the survey.

Survey Development and Design

The survey was developed by pediatricians, pediatric allergists, and health services researchers, with support of an expert panel composed of leaders in the field. For a detailed description of survey methodology, see Gupta et al.¹ The final survey was administered electronically and is available on request. Items assessed participant report of a child's food allergies, including date of onset, method of diagnosis, and reaction history for each reported allergen. Detailed demographic information, including household zip code, was also collected.

Study Participants and Recruitment

Eligible participants included adults (≥ 18 years) able to complete the survey in Spanish or English residing in US households with at least 1 child younger than 18 years. Participants were instructed to complete the survey for a child in their household randomly selected by survey algorithm. Recruitment was conducted using a dual-sample approach, in which a probability-based sample statistically representative of US households with children was used to identify and correct for sampling and nonsampling bias introduced by a larger, opted in online sample. Recruitment and weighting schemes are described in depth in Gupta et al.¹

Outcome Measures

The primary outcome measure was food allergy prevalence. Only food allergies reported to induce one or more of the following reaction symptoms were included in the analysis: anaphylaxis (defined as a severe allergic reaction that can lead to death), angioedema of lips/eyes/face, other angioedema, coughing, other oropharyngeal symptoms, eczema, flushing, hives, low blood pressure, pruritus, trouble breathing, vomiting, or wheezing. Among cases included in the analysis, 70.4% (95% confidence interval [CI] = 67.9-72.7) also included report of physician diagnosis with serum specific IgE testing, skin prick testing, or an oral food challenge.

A food allergy was categorized as mild-moderate or severe based on reaction history. Mild-moderate symptoms were limited to angioedema of lips/eyes/face, other angioedema, coughing, other oropharyngeal symptoms, eczema, flushing, hives, pruritus, and vomiting. Severe symptoms included any report of anaphylaxis, low blood pressure, trouble breathing, or wheezing. A

reaction including vomiting, angioedema, and coughing in combination was also categorized as severe.

Statistical Analysis

All summary statistics were weighted using both base and poststratification weights to adjust for potential biases from sampling design and survey response as described in Gupta et al.¹ Geographic characteristics were assessed using multiple parameters, including state, latitude, and urban/rural status. Latitude was assigned by zip code and collapsed into 3 quantiles: northern ($\geq 41.8^\circ$ N latitude), middle (34.3° N to 41.7° N latitude), and southern ($\leq 34.2^\circ$ N latitude). Urban/rural status was assigned by zip code using the Rural-Urban Commuting Area Codes (RUCA) version 2.0, created based on 2000 Census commuting data and 2004 ZIP codes by University of Washington Rural Health Research Center (<http://depts.washington.edu/uwruca/index.php>). The original 38 rural/urban groups were collapsed into the following geographic areas, from highly urbanized to very rural: urban centers, metropolitan cities, urban outskirts, suburban areas, small towns, and rural areas..

Demographics and prevalence estimates were calculated using weighted proportions. Data summary were implemented in SAS callable SUDAAN 10.1. ArcGIS 10 was used to map the state-level child food allergy prevalence. Multiple logistic regression models, adjusted for survey design and sample weights, were estimated to examine the association of urbanization with status of food allergy and food allergy severity. Models were adjusted for demographic characteristics and latitude. A type I error of $< .05$ was used to evaluate the significance of statistical associations. Statistical models were estimated with SAS 9.2.

Results

Data were collected for 40 104 children. Incomplete responses for 1624 children were not included in the analysis. Data for an additional 15 children could not be coded into geographic areas, yielding a final sample of 38 465.

Half of all children were male (51.1%), with a mean age of 8.5 years (95% CI = 8.5-8.6). Race/ethnicity was mutually exclusive, with 56.4% of children reported to be White, 21.5% Hispanic, 14.2% Black, and 4.8% Asian. Demographic characteristics by geographic area are presented in Table 1.

The distribution of food allergy across the United States is shown in Figure 1. Odds of food allergy were significantly *higher* at more southern and middle

Table 1. Demographic Characteristics of All Children Surveyed by Geographic Area (N = 38 465)

Variable	Frequency, % (95% Confidence Interval)					
	Urban Centers (N = 3124)	Metro Cities (N = 7560)	Urban Outskirts (N = 6782)	Suburban Areas (N = 11 546)	Small Towns (N = 1592)	Rural Areas (N = 7861)
Race/ethnicity						
Asian, non-Hispanic	11.7 (10.0-13.4)	7.5 (6.6-8.3)	3.5 (2.9-4.1)	4.2 (3.7-4.8)	1.9 (0.9-2.9)	1.3 (0.9-1.7)
Black, non-Hispanic	22.5 (19.9-25.2)	18.9 (17.2-20.7)	16.4 (14.7-18.1)	11.0 (9.9-12.1)	7.5 (5.1-9.8)	8.7 (7.6-9.8)
White, non-Hispanic	22.7 (20.7-24.7)	48.3 (46.4-50.1)	48.2 (46.1-50.3)	64.3 (62.8-65.9)	71.1 (67.2-74.9)	76.7 (75.1-78.3)
Hispanic	40.0 (36.9-43.1)	22.3 (20.5-24.0)	29.2 (26.9-31.6)	17.4 (16.0-18.7)	16.4 (13.2-19.6)	10.4 (9.1-11.7)
Multiple/other	3.0 (2.4-3.6)	3.1 (2.7-3.5)	2.7 (2.3-3.0)	3.1 (2.8-3.5)	3.2 (2.2-4.3)	2.9 (2.5-3.4)
Gender						
Female	48.0 (45.7-50.3)	49.9 (48.5-51.4)	47.8 (46.1-49.5)	49.0 (47.8-50.2)	48.5 (45.5-51.6)	49.6 (48.2-51.0)
Male	52.0 (49.7-54.3)	50.1 (48.6-51.5)	52.2 (50.5-53.9)	51.0 (49.8-52.2)	51.5 (48.4-54.5)	50.4 (49.0-51.8)
Age (years)						
0-2	18.5 (16.5-20.4)	16.9 (15.6-18.1)	16.9 (15.6-18.1)	15.9 (14.9-16.8)	18.0 (15.4-20.7)	15.6 (14.5-16.6)
3-5	16.5 (14.8-18.2)	18.1 (16.9-19.3)	18.1 (16.9-19.3)	17.0 (16.1-18.0)	16.6 (14.1-19.1)	15.9 (14.9-17.0)
6-10	26.1 (24.1-28.1)	26.0 (24.6-27.4)	26.0 (24.6-27.4)	27.4 (26.4-28.5)	26.1 (23.4-28.9)	26.9 (25.6-28.1)
11-13	17.3 (15.5-19.0)	17.4 (16.2-18.5)	17.4 (16.2-18.5)	17.1 (16.3-18.0)	17.7 (15.4-19.9)	17.7 (16.6-18.7)
14-17	21.7 (19.8-23.5)	21.6 (20.4-22.9)	21.6 (20.4-22.9)	22.5 (21.5-23.5)	21.6 (19.2-23.9)	24.0 (22.8-25.1)
Household income (\$)						
<25 000	23.3 (20.9-25.7)	24.3 (22.6-26.0)	24.3 (22.6-26.0)	13.2 (12.2-14.2)	30.2 (27.1-33.2)	25.1 (23.7-26.5)
25 000-49 999	27.0 (24.9-29.2)	30.7 (29.1-32.3)	30.7 (29.1-32.3)	25.6 (24.4-26.7)	35.0 (31.9-38.2)	33.6 (32.3-35.0)
50 000-99 999	29.6 (27.6-31.7)	31.0 (29.5-32.5)	31.0 (29.5-32.5)	40.6 (39.4-41.8)	28.4 (25.7-31.1)	33.2 (31.9-34.5)
100 000-149 999	13.3 (11.6-15.0)	10.5 (9.4-11.6)	10.5 (9.4-11.6)	15.1 (14.2-16.0)	5.5 (3.9-7.1)	6.3 (5.6-7.0)
≥150 000	6.8 (5.6-8.0)	3.5 (2.9-4.1)	3.5 (2.9-4.1)	5.6 (5.0-6.2)	0.9 (0.4-1.4)	1.8 (1.4-2.1)

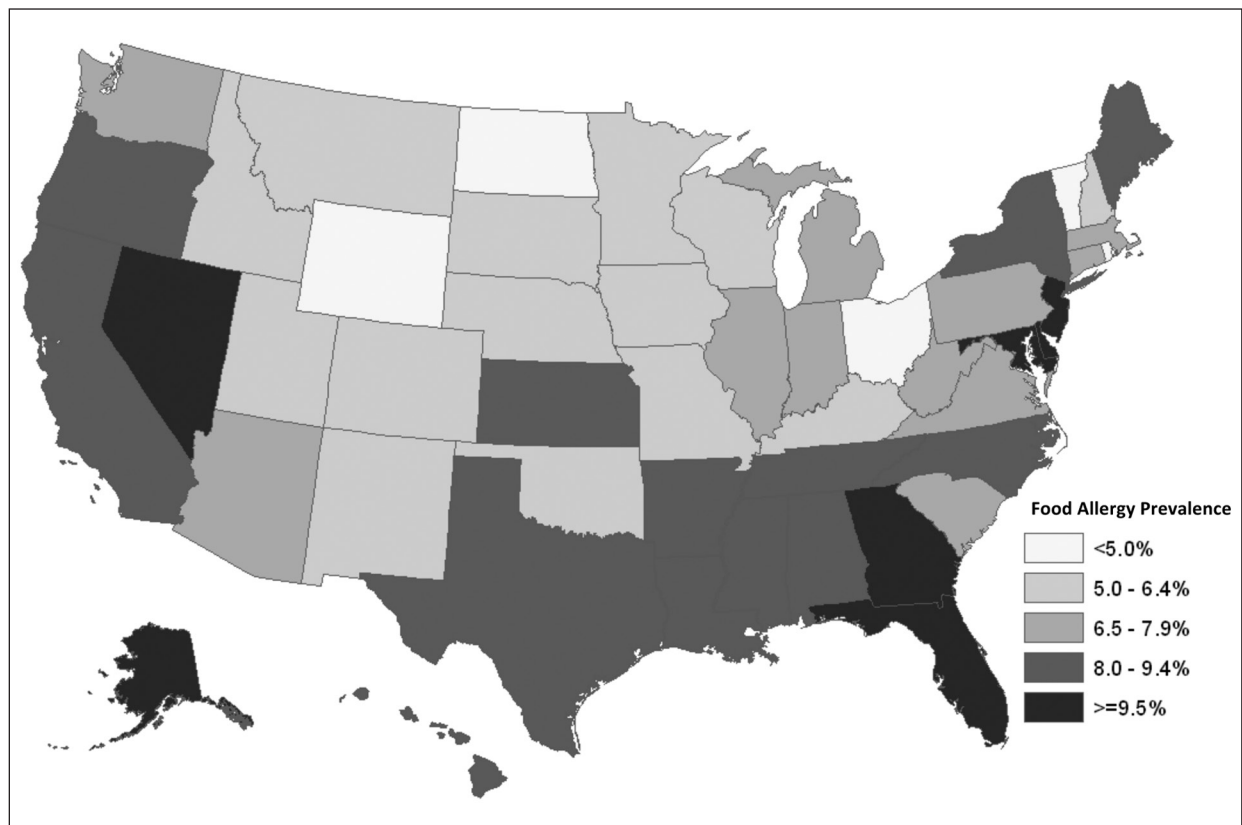
**Figure 1.** Distribution of childhood food allergy in the United States (N = 38 465)

Table 2. Food Allergy Prevalence by Geographic Area: Overall and by Common Allergen

Area	Frequency, % (95% Confidence Interval)								
	All Allergens	Peanut	Shellfish	Milk	Fin Fish	Egg	Tree Nut	Wheat	Soy
Urban centers	9.8 (8.6-11.0)	2.8 (2.2-3.5)	2.4 (1.8-3.0)	1.8 (1.4-2.4)	1.8 (1.4-2.3)	1.3 (0.9-1.8)	1.2 (0.8-1.6)	0.8 (0.5-1.1)	0.6 (0.3-0.9)
Metro cities	9.2 (8.4-10.1)	2.4 (2.0-2.9)	1.4 (1.1-1.8)	1.8 (1.5-2.2)	0.9 (0.6-1.2)	1.0 (0.7-1.3)	1.3 (1.0-1.7)	0.9 (0.7-1.2)	0.4 (0.3-0.6)
Urban outskirts	7.8 (7.0-8.6)	1.8 (1.5-2.3)	1.5 (1.2-2.0)	1.4 (1.1-1.7)	0.8 (0.5-1.1)	0.5 (0.4-0.8)	1.0 (0.8-1.3)	0.4 (0.3-0.6)	0.4 (0.2-0.6)
Suburban areas	7.6 (6.9-8.2)	2.0 (1.7-2.4)	1.2 (1.0-1.5)	1.5 (1.2-1.8)	0.7 (0.5-0.9)	0.7 (0.5-0.9)	1.2 (0.9-1.5)	0.8 (0.6-1.0)	0.3 (0.2-0.5)
Small towns	7.2 (5.7-8.6)	1.6 (1.0-2.6)	1.0 (0.6-1.7)	1.4 (0.9-2.3)	0.5 (0.3-1.0)	0.7 (0.4-1.4)	0.9 (0.6-1.6)	1.1 (0.7-1.9)	0.5 (0.2-0.9)
Rural areas	6.2 (5.6-6.8)	1.3 (1.0-1.6)	0.8 (0.6-1.1)	1.5 (1.2-1.8)	0.2 (0.1-0.4)	0.5 (0.3-0.7)	0.6 (0.4-0.8)	0.5 (0.3-0.7)	0.2 (0.1-0.4)
P	<.0001	<.0001	<.0001	.3993	<.0001	.0045	.0001	.0040	.2658

Table 3. Odds of Food Allergy and Severe Versus Mild/Moderate Food Allergy by Geographic Area: Adjusted for Race/Ethnicity, Gender, Age, Household Income, and Latitude

Area Versus Rural	Odds of Food Allergy		Odds of Severe Food Allergy	
	Unadjusted	Adjusted	Unadjusted	Adjusted
Urban centers	1.7 (1.5-2.0)	1.5 (1.3-1.8)	1.4 (1.0-1.8)	1.3 (0.9-1.8)
Metro cities	1.5 (1.3-1.7)	1.4 (1.2-1.6)	1.1 (0.9-1.5)	1.1 (0.8-1.4)
Urban outskirts	1.3 (1.1-1.5)	1.2 (1.1-1.4)	1.0 (0.8-1.3)	1.0 (0.8-1.3)
Suburban areas	1.2 (1.1-1.4)	1.2 (1.0-1.3)	1.1 (0.9-1.4)	1.0 (0.8-1.3)
Small towns	1.2 (0.9-1.4)	1.2 (0.9-1.5)	1.2 (0.8-1.8)	1.1 (0.7-1.7)

latitudes compared with northern latitudes (odds ratio [OR] = 1.5, 95% CI = 1.3-1.8 and OR = 1.3, 95% CI = 1.1-1.5, respectively), suggesting a north-to-south increase in the rate of food allergy.

Prevalence rates varied significantly from 9.8% in urban centers to 6.2% in rural areas (Table 2). Prevalence rates for specific allergens also varied significantly by urban/rural status. Only milk and soy allergy appeared to affect a similar proportion of children regardless of geographic area. Peanut was consistently among the 2 most common allergens and was first in all but rural areas, in which milk allergy was more common.

Odds of food allergy were significantly higher in more densely populated areas, even after adjusting for demographic characteristics and latitude (Table 3). Odds were graded such that odds of food allergy in urban centers versus rural areas were highest, followed by metro cities versus rural areas, and so on. A significant difference in odds of food allergy was not observed between small towns and rural areas, in either the unadjusted or

adjusted model. Odds of severe food allergy did not differ significantly by urban/rural status or latitude.

Discussion

Food allergy prevalence was found to vary by urban/rural status, even after controlling for potential confounders, including race/ethnicity, household income, and latitude. Increasing population density corresponded with increasing prevalence rates, with 9.8% of children affected in urban centers compared to 6.2% of children in rural areas. Significant variation was also observed by allergen, with only milk and soy affecting a similar proportion of children in all areas. Severity of allergy, however, did not show a strong association with area of residence.

To our knowledge, an urban/rural difference in food allergy prevalence has not been previously reported in the United States. However, in Australia, geographic remoteness has been significantly associated with decreased sales of infant hypoallergenic formulas and

EpiPen prescriptions—proxies for food allergy prevalence—even after adjusting for socioeconomic status, latitude, and access to care.¹⁸ Also consistent with our data, the latter study found no significant association between geographic remoteness and anaphylaxis admission rates—a proxy for food allergy severity.¹⁸ Such data suggest that urban/rural status may play a role in allergen sensitization without influencing morbidity.

Although there is a paucity of literature on urban/rural status and food allergy, past work clearly demonstrates an association between urban/rural status and comorbid atopic diseases, including asthma, eczema, allergic rhinitis, and allergic conjunctivitis.¹³⁻¹⁷ Many theories have been proposed to explain urban–rural differences in atopic disease, and may likewise apply to urban-rural differences in food allergy. Among them, the hygiene hypothesis suggests that exposure in early life to certain microbial agents associated with rural living may protect against atopy.^{19,20} Alternatively, the many ambient pollutants encountered in urban areas have been implicated in the pathogenesis of atopic disease.²¹

Odds of food allergy were higher at more southern latitudes, suggesting a north-to-south increase in prevalence rates. This finding is at odds with the few studies investigating geographic food allergy trends in the United States.¹⁰⁻¹² An observed decline in the rate of EpiPen prescriptions and food-induced allergic reactions from north-to-south in these studies was interpreted as support for a role of vitamin D deficiency in the pathogenesis of food allergy.¹⁰⁻¹² However, an alternative theory suggests that vitamin D may induce T helper 2 cell differentiation.²² In food allergy, the T helper 2 cytokine IL-4 induces B cell production of IgE.²³ Thus, it is possible that excess D₃, rather than deficiency, may contribute to our observed increase in food allergy with proximity to the equator.

Limitations to this study need to be highlighted. Reaction history and diagnosis of food allergy were based on participant report, which is subject to recall bias. Also, data on the reproducibility of reaction symptoms were not collected. However, the prevalence of a number of specific allergies is consistent with that reported by other studies (see Gupta et al¹), lending credibility to the definition of food allergy used in this study.

In summary, food allergy prevalence varied widely throughout the United States. An association between urban/rural status and prevalence of food allergy was observed. Prevalence rates increased steadily with increasing population density, from 6.2% in rural areas to 9.8% in urban centers. Although such a distribution has not been previously reported in the United States, studies of comorbid atopic conditions show similar urban–rural differences and provide insight into factors

which may be at work in food allergy. Understanding the influence of geography on the pathogenesis of food allergy holds promise for the treatment and management of disease and warrants further investigation.

Acknowledgments

The authors would like to thank the Food Allergy Initiative and Dave and Denise Bunning for their support of this research. Additionally, special thanks to Drs Xiaobin Wang, MD, MPH, ScD, and Rajesh Kumar, MD, of the Smith Child Health Research Program at Children's Memorial Hospital in Chicago, Illinois, for their valuable guidance in data analysis and article review.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: The Food Allergy Initiative, New York, NY.

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