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Peanut allergy diagnoses among children residing in Olmsted County, MN

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Abstract

Background—Peanut allergy is a major health concern particularly in developed countries. Research indicates that as many as 2% of children are allergic to peanuts, which represents a 3.0-fold increase in diagnoses over the last two decades.

Objective—This population-based descriptive study utilized the Rochester Epidemiology Project (REP) to estimate the prevalence in 2007 and annual incidence rates of peanut allergy diagnoses from 1999–2007 among children residing in Olmsted County, MN.

Methods—Residents of Olmsted County from January 1, 1999 through December 31, 2007 who received medical care at a REP facility and provided research authorization were eligible for the study. A medical chart review of 547 potential diagnoses resulted in 244 prevalent and 170 incident cases. Annual rates, crude and adjusted for age and gender, were standardized using the indirect method to the Olmsted County population data in 1999. Incidence rate ratios were estimated using Poisson regression.

Results—The prevalence in 2007 was 0.65%. Female children were less likely to be diagnosed than male children (IRR=0.18 95% CI (0.07,0.48)). Children aged 0–2 years were significantly more likely to be diagnosed than older children aged 3–17 years old (IRR=0.001 95%CI (0.0004,0.004)). There was a significant 3-fold increasing trend in diagnoses over time from 2.05 cases per 10,000 children in 1999 to 6.88 cases per 10,000 in 2007.

Conclusions—Peanut allergies are an increasing concern in Olmsted County, MN as indicated by a 3-fold increase in diagnoses from 2.05/10,000 children in 1999 to 6.88/10,000 children in 2007.

Keywords

Peanut allergy; Children; Incidence; Prevalence; Olmsted County; Rochester Epidemiology Project

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INTRODUCTION

Food allergies affect approximately 8% of children in the United States ¹⁻³. The most common foods inducing clinical reactions are cow's milk, wheat, egg, soy, peanut, tree nuts, fish and shellfish ¹⁻³. Peanut allergy is an immunoglobulin E (IgE) mediated hypersensitivity reaction to peanut proteins. The allergy typically presents early in life and only a minority of cases resolve (20%) ⁴. Reactions to peanut represent the majority of cases of food-induced anaphylaxis ⁵. In highly sensitive people, trace quantities can induce severe allergic reactions ⁵. Currently, the only available treatment is strict avoidance, recognition of early symptoms of a reaction and usage of emergency medication ⁶.

Peanut allergy is a major health concern particularly in developed countries in which as many as 2% of children are allergic ⁷. Considerable variability exists in regards to published prevalence estimates, which range from 0.5% to 2.0%, and among studies examining changes in prevalence and incidence rates over time, with some estimates indicating a 2.0–3.0-fold increase over the last decade ⁸⁻²². Specifically, studies from the United States report a significant increase in self-reported allergy from 0.4% in 1997 to 1.4% in 2008 ⁹⁻¹¹. Research conducted in the United Kingdom reports a significant increase in clinical allergy, defined as evidence of sensitization in conjunction with an adverse reaction to peanut, from 1989 (0.5%) to 1996 (1.4%) and a non-significant decrease in 2003 (1.2%) ¹²⁻¹⁴. Further, studies conducted in Canada report a non-significant increase in clinical allergy from 1.34% in 2002 to 1.62% in 2007 ^{15,16}. Lastly, an Australian study reports a significant 2.5-fold increase in incidence rates from 1995 (0.47%) to 2007 (1.15%) ¹⁷.

The results from these studies are difficult to compare and interpret in the aggregate due to the variability in results, which is likely due to a lack of uniformity in the criteria utilized to define peanut allergy and methods used to identify peanut allergic individuals. Identification of cases based on parental self-report or evidence of sensitization alone as opposed to reliance on the gold standard for diagnosis, food challenges, or evidence of clinical allergy as indicated in medical records are known to produce inflated estimates of true allergy ⁶. There is a paucity of studies that utilize food challenges to enumerate the prevalence and incident rates of diagnoses over time. As a result, research that identifies cases based upon diagnostic criteria outlined by the current guidelines, as opposed to self-report or evidence of sensitization alone, is needed to produce accurate estimates for true allergy. This information will contribute to findings of other studies using similar methodology with the hope of growing a comparable, accurate, reproducible knowledge base ⁶.

METHODS

The prevalence of peanut allergy in 2007 and annual incidence rates from 1999–2007 among children were estimated using data obtained from the Rochester Epidemiology Project (REP) ^{23,24}. The REP is a population-based medical records linkage system in which medical diagnosis data from the primary providers of care in Olmsted County are linked to individual patients. The largest provider of care is the Mayo Clinic, which has maintained a common medical record with its two large affiliated hospitals, St. Mary's and Rochester Methodist since 1907. Mayo's indexing system was later extended to the other providers in Olmsted County including Olmsted Medical Center, its affiliated hospital and the Rochester Family Medical Center. A Target store outpatient clinic and a nurse practitioner's office are the only providers of medical care in Olmsted County that do not participate in the REP.

The REP is an excellent representation of the Olmsted County population. Ninety-eight percent of Olmsted County residents seen from 1998–2007 granted permission for at least one of their medical records to be used for research and ninety-one percent granted

permission for all of their records to be used for research²³. Further, as compared to 2000 U.S. Census population estimates for Olmsted County, the REP more closely estimated the population aged less than 18 years than did the U.S. Census²³.

All diagnoses and surgical procedures from these facilities were numerically coded using either the Hospital Adaptation of the International Classification of Diseases, Second Edition, or the International Classification of Diseases, Ninth Revision, coding systems. These codes are indexed for computerized retrieval. Using this retrieval system, a search was conducted for all patients who had a new diagnostic code related to peanut allergy from 1999 through 2007, were residents of Rochester, Minnesota and who gave permission for their medical records to be used for research.

A list of patients with a potential diagnosis of peanut allergy in the medical records from 1999–2007 was generated and the medical charts were reviewed to confirm cases of peanut allergy. Specifically, the medical records for 547 patients with codes representing the following diagnoses were reviewed: allergy food, allergy food with dermatitis, allergy peanuts, allergy food personal history, allergy peanuts personal history, anaphylaxis shock peanuts, anaphylaxis, and allergic reaction. Patients who met the criteria for a diagnosis of peanut allergy, as defined below, were included in the study.

Specifically, to be considered allergic to peanuts, each patient had to meet criterion 1, as outlined below, and at least one of criteria 2–4⁶.

1. Positive history of an IgE mediated type 1 hypersensitivity reaction AND
2. A positive blood test result (≥ 0.35 kU/l) OR
3. If blood testing is negative, positive skin prick test (> 3.0 mm) OR
4. If both blood and skin prick testing are negative, a positive food challenge

The Mayo Foundation, Olmsted Medical Center and University of Minnesota institutional review boards approved the study.

Study Population

Subjects who did not provide permission for their medical records to be used for research, whose residency information was not available, who were not residents of Olmsted County at the time of diagnosis and/or did not meet the diagnostic criteria for peanut allergy were excluded from the data set. The complete medical records of each potential subject were reviewed to confirm a case of peanut allergy and collect information regarding demographics, health status, presenting symptoms, and outcome. Of the 547 potential cases, 171 (31.3%) unique incident cases were identified who met the diagnostic criteria during 1999–2007. Twelve duplicate cases were eliminated from the original sample of 183 cases, which resulted in 171 unique incident cases. From the sample of 171 incident cases, 1 case was eliminated due to incorrect date information that could not be verified. The final analytic sample for incident rate calculations consisted of 170 cases. All data were abstracted using an electronic data collection form.

Prevalence

A prevalent case was defined as an Olmsted County resident that was a patient of a REP facility from 1999–2007 with a diagnosis of peanut allergy. Prevalent cases are a mixture of existing and new cases of peanut allergy diagnosed in the medical records from 1999–2007. Thus, the allergy may have been diagnosed prior to 1999 and may or may not have been initially diagnosed at a REP facility. It is estimated that approximately 20% of people with peanut allergy diagnosed before the age of five years will become tolerant of peanuts. The

medical records of all cases were followed in time to determine whether they became tolerant of peanuts and if so, the subject was removed from the prevalence estimate by subtracting that case from the numerator total.

Incidence

An incident case was defined as a new diagnosis of peanut allergy made at a REP facility from 1999–2007 in an Olmsted County resident.

Tolerance

A child was considered to have become tolerant to peanuts if they were previously diagnosed as peanut allergic, per study definition, and subsequently passed an in office food challenge ⁶.

Statistical Analysis

Participant characteristics of all cases were descriptively summarized by means and standard deviations for continuous variables or by frequencies for categorical variables. These characteristics included age of first diagnosis, year of first diagnosis, and gender.

An estimate of the prevalence of peanut allergy in 2007 was calculated by dividing the numerator, all prevalent and incident cases of peanut allergy in the medical records from 1999–2007 minus those children who acquired tolerance, by the denominator, the Olmsted County population aged less than 18 years estimated from US census data. In calculating incidence rates, the entire population of Olmsted County age 17 years or less was considered at risk. The overall denominator, as well as age- and gender-specific person-years, were estimated from decennial census data with linear interpolation between census years

The incident diagnosis for each case contributed to the numerator for the incidence rate calculation for that respective year. Annual rates, crude and adjusted for age and gender, were standardized using the indirect method to data in 1999 for Olmsted County. Using indirect methods is preferred when rates are unstable due to rare events. A test for trend was conducted to assess whether there was a statistically significant increase in the annual age- and gender-adjusted rates of peanut allergy diagnoses over time.

Poisson regression was used to estimate incidence rate ratios using log of person-time offset to examine the multivariable relationship of incidence rates with age, gender and diagnosis year. The denominator for the incident rate calculation was estimated using the log of person-years. In each year, the time at risk for those with a peanut allergy diagnosis was estimated as the time until they were diagnosed (i.e. A person who was diagnosed in March 1999 would contribute 0.25 person-years). For the rest of the population in that year with no disease, it was assumed they contributed one-person year. All data were analyzed in SAS 8.0 software.

RESULTS

There were 244 prevalent cases of peanut allergy among children aged less than 18 years in Olmsted County, MN from 1999–2007. Seven cases developed tolerance. Thus, the final prevalence estimate in 2007 was 237 cases/36,312 (the Olmsted County, MN population of children in 2007) or 0.65%.

There were 170 incident cases of peanut allergy over this time period (Table 1). The majority of children were 0–2 years (77.7%) and male (69.4%). The number of incident

cases of peanut allergy increased overall from 1999–2007 with 5.9% of new diagnoses in 1999 and 17.7% in 2007.

As seen in Figures 2 and 3, the age- and gender-adjusted rates increased three-fold from 2.05 cases per 10,000 children in 1999 to 6.88 cases per 10,000 children in 2007 overall with rises and falls throughout the years. A test for trend was conducted to determine whether the annual age- and gender-adjusted rates of peanut allergy diagnoses increased statistically over time. The results indicated that there was a significant increase in peanut allergy diagnoses over time from 1999–2007 ($p=0.005$).

Figures 2 and 3 present annual rates, age and gender-adjusted and age and gender standardized, using the indirect method to the 1999 Olmsted County population. Overall, rates of allergy in females were lower than the rates in males each year (Figure 2). Further, the rates are the greatest in the 0–2 year age category as compared to the older groupings (Figure 3). The figures represent an overall rise in rates from 1999–2007 among both genders and age groups.

The multivariable analyses, as seen in Table 2, indicated that females had a statistically significant 82% lower rate of peanut allergy diagnosis as compared to males after adjustment for age and year of diagnosis (IRR=0.18 95% CI (0.07,0.48)). Furthermore, the rate ratio for disease, peanut allergy diagnosis, increased over time as compared to the reference years, 1999–2001. Rates for peanut allergy diagnosis in 2002–2004 and 2005–2007 as compared to 1999–2001 are 2.13 (95% CI 0.61,7.41) and 5.15 (95% CI 1.63,16.3) times greater respectively, after adjustment for gender and age of diagnosis with only the years 2005–2007 indicating a significant association with peanut allergy rate. With regards to age, as compared to children aged 0–2 years old, older children aged 3–17 years have a 99.9% significantly lower rate of peanut allergy diagnosis after adjustment for year of diagnosis and gender. In multivariable analyses, age, gender, and year of diagnosis remained significantly associated with incident peanut allergy (Table 2).

DISCUSSION

The analysis indicates that the 2007 prevalence of peanut allergy in this sample was 0.65%, while the incidence increased three-fold from 2.05/10,000 in 1999 to 6.88/10,000 in 2007. Males and younger children (0–2 years of age) were significantly more likely to be diagnosed with peanut allergy compared to older children (3–17 years) and females.

Our 0.65% prevalence is within reported ranges yet, slightly lower than estimates of clinical allergy and much lower than estimates based on sensitization alone^{7–22}. Sensitization is not an accurate estimation of clinical allergy and thus, estimates of sensitization are expected to be much higher than those of clinical allergy, such as reported by this study⁶.

Our data suggest that there has been a statistically significant increase in peanut allergy diagnoses over time in this population. The age- and gender-adjusted rates of peanut allergy diagnoses increased three-fold from 2.05 cases per 10,000 children in 1999 to 6.88 cases per 10,000 children in 2007, which is consistent with other reported studies^{7–22}. Further, peanut allergy diagnoses in the year range 2005–2007 as compared to 1999–2001 indicated a significant association with peanut allergy rate whereas the earlier years 2002–2004 did not. The significant increase in diagnoses in more recent years is consistent with other reported studies^{7–22}. The cause for this increase is under investigation and was not assessed in this study.

The analysis indicates that females were significantly less likely to experience a peanut allergy diagnosis than male children, with 69.4% of cases found to be male. The literature

indicates that the prevalence of peanut allergy is greater among males than females with reported estimates in the range of 63%–69%^{7–22}. It is established that rates of atopic diseases differ according to gender²⁵. In population-based studies, these differences, assessed as skin test reactivity to one or more of a panel of allergens, have been reported throughout childhood and into early adulthood²⁵.

Children aged 0–2 years were significantly more likely to be diagnosed with peanut allergy compared to older children aged 3–17 years. This conclusion is consistent with reported studies and is expected as the introduction of new foods typically begins in this age range and if a reaction were to occur, it would be expected to surface at this time^{7–22}.

Using the REP to collect retrospective data for this study produced reliable information pertaining to this specific geographical area. Variations in numbers reported by other studies from other geographical areas create hypothesis-generating comparisons. Future prospective studies would also achieve high quality data and interesting results.

Strengths

The proposed study has a number of strengths, which allow accurate classification and enumeration of peanut allergic cases in this population. The study takes advantage of the population based medical data available through the Rochester Epidemiology Project resources²⁴. This linked medical records system enables access to accurate and detailed clinical and laboratory data over many years, which minimizes misclassification bias. Further, due to the nature of the referral system for care in Olmsted County, cases received a final diagnosis of peanut allergy from a physician trained in pediatric allergy. In addition, changes in diagnostic classification during the study period are unlikely to have impacted study results due to the nature of the retrieval system led by experts in proper case enumeration. Lastly, the REP enumeration of the Olmsted County population closely matches that of the U.S. census and 98% patients receiving care at one of the REP facilities consented to inclusion of their medical records into the database²³. Thus, the patients captured in this medical record review are representative of the Olmsted County population.

Limitations

The results of this study may vary from the true population prevalence and/or incidence due to a few potential reasons. There are several instances in which a case of peanut allergy may not have been counted because of the conservative case definition used in this study. For instance, a child who is labeled as peanut allergic in the medical records yet has no evidence of confirmatory testing was not considered a case. Also, a child who tested positive for peanut allergy yet, had never ingested peanuts was not considered a case. A sensitivity analysis was conducted to enumerate potentially missed cases, which indicated that there were 63 possible cases. Including potential misses in the assessment increased the prevalence estimate to 0.83% 300 cases /36,312 children).

In addition, the possibility exists that an incident event was improperly classified as a first time diagnosis leading to an overestimation of incidence. Every effort was made to review all medical records to be sure that each incident event was in fact the first time diagnosis. Third, cases only include those people that seek medical care for their condition and does not include those that self-diagnosis and avoid peanuts. Therefore, the results reflect physician-diagnosed cases, which may not capture all cases in a population.

Tolerance was defined in this study as confirmation of acquiring oral tolerance through an in office food challenge, which is in accordance with the guidelines⁶. There were several instances in which a child's allergy testing levels became negative yet, there was no indication in the medical charts of a confirmatory food challenge. Further, many of these

cases did not have any additional allergy or medical visits pertaining to peanuts. This subset of children may have acquired tolerance however, this could not be confirmed through documentation of passing an in office food challenge and thus could not be included in our tolerance count. Therefore, our tolerance count may be low and therefore, our prevalence slightly high.

A recent study estimated the prevalence of general practitioner recorded diagnosis of peanut allergy in the English population in 2005 (0.51 per 1000 patients) ²⁵. The prevalence estimate was lower than other reports, which the authors believed was a result of under recording in general practice ²⁶. It is not likely that under recording affected the results of this study. The Mayo Clinic is a unique institution in which the close work environment between general practitioners and specialists in conjunction with the electronic medical records system makes under coding of diagnoses infrequent ^{23,24}.

Every effort was made to ensure that the list of diagnostic codes used to identify cases was complete. The list of codes, which were used as the search criteria to identify cases of peanut allergic children, was compiled in consultation with pediatric allergists at the Mayo Clinic who counsel patients and code diagnoses daily. Therefore, it is unlikely that missed diagnostic code(s) affected the prevalence estimate.

The sample size of this study is small and as such the results must be interpreted cautiously. Further, in comparison to the 2000 US Census data, Olmsted County was shown to be less ethnically diverse, more highly educated and wealthier than the US population, which may limit extrapolation of results outside this geographic area ²³. In addition, research indicates that latitude may influence the prevalence of food allergies in a population ²⁷. Olmsted County, MN is a northern community in which vitamin-D levels obtained through sun exposure are potentially lower than those found in children in more southern communities. This factor may contribute to the prevalence estimates reported but was not evaluated. Lastly, the rise in incident cases may be due to an increased awareness of peanut allergies by patients and/or physicians, both of which the study did not assess.

Conclusions

Among children residing in Olmsted County, MN, the prevalence of peanut allergy in 2007 was 0.65% and the incidence rate increased 3-fold from 2.05/10,000 children in 1999 to 6.88/10,000 children in 2007. The results provide important data to Olmsted County, MN clinicians in terms of patient counseling and management. For instance, clinicians may explain to patients that 0.65% of children are diagnosed with their condition, which has increased three-fold over the last decade. Further, an accurate indication of the number of peanut allergic children is significant to Olmsted County public health practitioners in preparation for awareness, safety and educational efforts. In conjunction with additional empirical support regarding the increasing prevalence of peanut allergies among children, enhanced perception of risk further supports efforts regarding enforcement of labeling laws and bans of peanuts in high-risk settings. Lastly, additional confirmation of an increase in rates further supports the need for research into etiology, prevention and therapeutic techniques.

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Abbreviations

IgE	Immuno-globin E
REP	Rochester Epidemiology Project
SPT	Skin prick test
kU/L	kilo-units per liter

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Clinical Implications

Peanut allergies are an increasing concern in Olmsted County, MN as indicated by a 3-fold increase in diagnoses from 2.05/10,000 children in 1999 to 6.88/10,000 children in 2007.

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Capsule Summary

Among children residing in Olmsted County, MN, the prevalence of peanut allergy in 2007 was 0.65% and the incidence rate increased 3-fold from 2.05/10,000 children in 1999 to 6.88/10,000 children in 2007.

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Figure 1.
Sample Size Waterfall

Figure 2.

Annual rates per 10,000 children, overall (age and gender adjusted) and gender specific rates standardized to the 1999 Olmsted County Population

Figure 3.

Annual rates per 10,000 children, overall (age and gender adjusted) and age-specific rates standardized to the 1999 Olmsted County Population

Table 1

Characteristics of Children in Olmsted County with Incident Diagnoses of Peanut Allergy from 1999–2007

Number of cases (n)	170
Age n (%)	
0–2 years	132 (77.7)
3–5 years	26 (15.3)
6–10 years	9 (5.29)
11–17 years	3 (1.76)
Gender n (%)	
Male	118 (69.4)
Female	52 (30.6)
Diagnosis Year n (%)	
1999	10 (5.9)
2000	11 (6.5)
2001	19 (11.2)
2002	10 (5.9)
2003	12 (7.1)
2004	28 (16.5)
2005	22 (12.9)
2006	28 (16.5)
2007	30 (17.7)

Table 2

Multivariable Adjusted Incidence Rate Ratios and 95% CI of Peanut Allergy Diagnosis by Year, Gender and Age

Variable	IRR	95% CI
Year		
1999–2001	Reference	
2002–2004	2.13	(0.61,7.41)
2005–2007	5.15	(1.63,16.3) *
Gender		
Male	Reference	
Female	0.18	(0.07, 0.48) *
Age		
0–2 years	Reference	
3–17 years	0.001	(0.0004,0.004) *

* Indicates a significant association (p<0.05)