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Food Allergy Sensitization and Presentation in Siblings of Food Allergic Children

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Abstract

Background—Many parents of food allergic children have concerns about the development of food allergies in their other children.

Objective—We sought to determine prevalence of food sensitization and clinical food allergy among siblings of food allergic children.

Methods—Two thousand eight hundred and thirty-four children were enrolled in the Chicago Family Cohort Food Allergy study. One thousand one hundred and twenty children (ages 0–21 years) with a food allergy (defined by a reported reaction history and evidence of food-specific IgE or skin prick test) and at least one biological sibling were included in this study.

Results—Among siblings of children with food allergy, 33.4% had no sensitization and no clinical symptoms to food. Fifty-three percent had a positive food serum-specific IgE or skin prick test, but no reported symptoms of food allergy. Only 13.6% of siblings were both sensitized and clinically reactive to the same food. Milk allergy was the most common allergy among siblings (5.9%), followed by egg allergy (4.4%) and peanut allergy (3.7%).

Conclusions—In a large cohort of food allergic families, only a small proportion of siblings were both sensitized and clinically reactive to a food. Sensitization without reactivity was common

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among siblings. Testing for food allergy in siblings without a history of clinical reactivity appears to be unjustified. Screening may lead to negative consequences related to potential misdiagnosis and unnecessary avoidance of a food. More data are needed to determine the absolute risk of food allergy development in siblings of food allergic children.

Keywords

Childhood food allergy; siblings; sensitization; skin testing, ImmunoCAP; milk allergy; peanut allergy; risk

INTRODUCTION

Food allergy is a growing public health concern impacting 8% of US children, 40% of which report having experienced symptoms of a potentially life-threatening reaction.¹ Given the absence of current preventative treatments for food allergy² beyond food avoidance, the ubiquity of food in our society, and the potentially fatal nature of reactions; food allergy has been associated with negative psychosocial impact, anxiety, and impaired health related quality of life (HRQL).^{2–12} Moreover, food allergic children managed with avoidance diets may experience nutritional deficiencies and growth impairment in addition to reduced HRQL.^{13,14}

A common concern for families is the degree of risk related to family history of food allergy and if siblings of food allergic children benefit from screening for food allergies prior to introducing potential allergenic foods. Multiple prevention guidelines suggest a bi-parental history of any allergic disease is a risk factor for developing food allergy, but few studies have investigated if family history can be better specified at the level of a specific family member (e.g., mother, father, or sibling).^{15–17} The available studies have been limited in scope to very few allergens (i.e., either solely focused on peanut allergy^{18–20}, or peanut, egg, and sesame allergy as a group²¹), were conducted in small numbers, and only two used OFC to confirm a reported food allergy. Current NIH guidelines state that there is insufficient evidence to recommend routine screening with specific immunoglobulin E (sIgE) or skin prick testing (SPT) before introducing commonly allergenic foods to any child, including siblings of food allergic children.² Serum specific IgE (sIgE) and skin prick tests (SPT) have poor precision in patients not previously exposed to the food (e.g. with no known history of ingestion, and thus a low pre-test probability for disease). The poor specificity and poor positive predictive value of these tests in such contexts may result in falsely positive results, potentially mislabeling many patients who are tolerant as allergic to the food allergen^{22–26} (i.e., sensitization to food versus true allergy to food). Such asymptomatic sensitization results may be over-interpreted, given a conservative sentiment towards potential food allergy, resulting in unnecessarily recommending such children avoid those specific foods, impairing the child^{13,14} and family's HRQL.^{2–12}

The Chicago Family Cohort is a large cohort formed to study genetic risk factors for food allergy among families with a food allergic child. Using nested data from within this large cohort, we sought to determine prevalence of food sensitization and clinical food allergy among siblings of food allergic children. We also aimed to understand potential factors

contributing to the development of food allergy and sensitization in siblings of food allergic children.

METHODS

Sample Recruitment

The 1,120 children included in this study were enrolled as part of The Chicago Family Cohort Food Allergy study. The enrollment process for this cohort is described elsewhere.²⁷ Families were recruited through general medical and allergy specialty clinics, community support groups and media advertisements. Participants were eligible for enrollment in the original cohort study if a parent of at least one biological child (ages 0–21 years) with food allergy was willing to fill out a detailed screening history for the child and family, as well as provide informed consent for the children in the family to undergo skin and serologic testing for food allergies. The present study included eligible families that had one index child with a confirmed food allergy and who had at least one sibling that participated in the study, for a total of 478 index children and 642 siblings. The Institutional Review Board of the Ann and Robert H. Lurie Children's Hospital of Chicago (formerly Children's Memorial Hospital) approved the study protocol. All participating families provided written informed consent to be a part of the Chicago Family Cohort Food Allergy study.

Data Collection

Trained research staff administered a structured questionnaire as part of the cohort enrollment interview to each parent about multiple risk factors for the development of food allergy. These included the child's history of asthma (parental report of a physician diagnosis of asthma), birth order and number of siblings, reported antibiotic use in the first year of life, reported infections (common cold, skin infections, respiratory syncytial virus), reported eczema, and pet ownership. Caregivers were also asked if the child was cared for outside of the home before age five and in what context (i.e. child care center/preschool, home-based childcare in someone else's home, home-based childcare in their own home). Mothers were asked if the child was breastfed, bottle fed or both and how long they exclusively breastfed. Both the older sibling(s) of an index child as well as the younger sibling(s) were included in the analysis.

Sensitization and Food Allergy Status

Specific IgE values for nine food allergens (egg white, sesame, peanut, soy, cow milk, shrimp, walnut, cod fish and wheat) were measured for each subject using the Thermo Fisher ImmunoCAP system (Thermo Fisher Scientific, Portage, MI, USA). The reported range for sIgE was from 0.1 (lower limit of detection) to greater than 100 kUA/L (upper limit of reporting), with >0.35 kUA/L considered positive. Specific IgE assays were performed by the Clinical Immunology Laboratory at Ann and Robert H Lurie Children's Hospital of Chicago, a CLIA-certified laboratory for the ImmunoCAP assay.

SPTs were performed on all eligible participants using the Multitest II device (Lincoln Diagnostics) to nine food allergen extracts (cow milk, egg white, soybean, wheat, peanut, English walnut, sesame seed, fish mix [cod, flounder, halibut, mackerel, tuna], and shellfish

mix [clam, crab, oyster, scallops, shrimp]), plus negative (50% glycerinated saline) and positive (histamine, 1.0 mg/mL) controls (Greer, Lenoir, NC, USA). The tests were placed on either the volar forearm or back (for young children) and results were measured 15 min after application. The test was considered positive if the mean wheal diameter was ≥ 3 mm than the saline control and the positive control wheal was at least 3 mm in diameter.

Food allergy status was determined by applying a set of clinical criteria to data gathered from the questionnaire-based interview performed by study staff and results of sIgE measurements and SPT. A set of stringent criteria was formed by a panel of study co-investigators who were attending physicians of the Division of Allergy and Immunology at Children's Memorial Hospital. The stringent criteria algorithm did not go through a formal validation process but has been used in other published studies.^{27–30} OFCs were not used to confirm clinical report of reactivity. Stringent clinical criteria indicative of highly likely clinical reactivity were met if a) the subject had evidence of sensitization (sIgE >0.35 kUA/L or prick skin test wheal >3 mm than the saline control to that food) and b) a reported history of typical symptoms of an allergic reaction to a food with onset within 2 hours of ingestion. Manifestations likely indicative of an IgE-mediated food allergic reaction included any one of the following: skin (hives or angioedema); respiratory tract (difficulty breathing, shortness of breath, repetitive coughing, wheezing, or chest tightness); oropharynx (throat tightness, choking, or difficulty swallowing; tongue swelling); cardiovascular system (fainting, dizziness, light-headedness, or decreased level of consciousness); or gastrointestinal tract (vomiting).

Criteria for severe food allergy among those meeting stringent criteria could be met in one of two possible ways. One, subjects could have reported symptoms of the skin, throat, mouth, or periorbital angioedema within two hours of exposure to the food and at least one manifestation of respiratory compromise or cardiovascular dysfunction as described above. Or two, subjects could have symptoms within two hours of exposure to the food affecting at least two of the following areas: (a) involvement of mouth, skin, throat, or periorbital area; (b) respiratory compromise; (c) cardiovascular dysfunction; or (d) gastrointestinal symptoms with vomiting. These criteria were developed in accordance with the 2006 National Institute of Allergy and Infectious Diseases (NIAID) and Food Allergy and Anaphylaxis Network (FAAN) criteria².

Statistical Analysis

Specific food allergen and overall food allergy prevalence rates within the population for both clinical food allergy and sensitization were calculated. To compare associations between allergies in the index child and their siblings, we used chi-squared tests. Because of the small sample size, we did not calculate adjusted risk ratios except for overall allergy. Multinomial logistic regression (with adjustment for clustering within families) was used to model potential associations between sibling characteristics and the odds of having sensitization or food allergy. All statistical analysis was done using STATA statistical software (StataCorp LP, 2013, College Station, TX).

RESULTS

Data were collected from 1,120 total children (both siblings and the index allergic child). Data for index children without siblings, children without food allergy, or those without complete data were not included in the analysis. In total, 642 siblings and 478 food allergic index children were included for analysis. The majority of the participants were male (63.6% of index children, 48.1% of siblings) and approximately half were between 2 to 5 years of age (50.0% of index children, 40.2% of siblings). Index children most commonly had one sibling (65.8%) -only 28.2% had two siblings, and 6% had three or more siblings. Overall, 66.5% of siblings were younger than the index child (Table I).

Rates of food sensitization among siblings

The prevalence of sensitization to any food without meeting criteria for food allergy among siblings was 53.0% (n=340). An additional 33.4% (n=215) of siblings had neither sensitization nor evidence of clinical food allergy. Wheat sensitization (36.5%, n=234) was the most common finding among the siblings, followed closely by milk sensitization (35.4%, n=227) and egg sensitization (35.1%, n=225) (Table II). Milk allergy in the index child was significantly associated with milk sensitization without history of milk reactivity in the sibling (27.2%, $p<0.01$).

Food allergy among siblings

Using the stringent grading criteria previously described, the prevalence of any food allergy among siblings was 13.6% (n=87). Among those with any food sensitization, 4-fold more siblings were sensitized without any clinical relevance than were food allergic. Specific food allergen prevalence among siblings was estimated in Table III. Milk allergy was the most common allergy (5.9%, n=38) among the siblings, followed by egg allergy (4.4%, n=28) and peanut allergy (3.7%, n=24). Milk allergy in siblings was significantly associated with both egg allergy ($p<0.01$), and peanut allergy ($p<0.05$) in the index child (Table III). Tree nut allergy in the index child was significantly associated with any sibling allergy ($p<0.01$), sibling egg allergy ($p<0.01$) and peanut allergy ($p<0.01$). In the adjusted results (Table IV), tree nut allergy was also significantly associated with overall allergy (RRR, 1.99; 95% CI 1.06–3.74; $p<0.01$). Siblings who were sensitized but not allergic had no reported reaction to the specific allergen in question. We excluded 81 children from our analysis because they did not meet the stringent criteria for food allergy.

Factors associated with the development of food allergy in the sibling

In unadjusted analysis, a reported history of skin infections in the first year of life (RRR, 6.49; 95% CI, 1.24–34.14; $p<0.05$), parental report of a provider diagnosis of asthma (RRR, 4.28; 95% CI, 2.38–7.70; $p<0.01$), and reported eczema (RRR, 4.80; 95% CI, 2.82–8.16; $p<0.01$) in the sibling were associated with an increased risk for developing food allergy (per the stringent criteria). However, in an adjusted multinomial regression (accounting for number of siblings, breastfeeding, asthma, eczema, skin infections, cats, dogs, age, common cold, RSV, paternal atopy, maternal atopy, gender, household income, antibiotics, race, and childcare), only a history of asthma (RRR, 4.14; 95% CI, 2.04–8.59; $p<0.01$) and eczema (RRR, 3.60; 95% CI, 2.04–6.34; $p<0.01$) were significantly associated with an increased risk

for food allergy among siblings (Table IV). While asthma was not significant associated with sensitization in the adjusted analyses, eczema was significantly associated with sensitization (RRR, 1.66; 95% CI, 1.12 – 2.45, $p < 0.05$).

DISCUSSION

In this large, established nested cohort, the majority (53%) of siblings of food allergic children were food sensitized but did not have clinical food allergy. An additional 33.4% of siblings were neither sensitized nor had evidence of clinical food allergy. Overall, only 13.6% of siblings had a clinically reactive food allergy. While this is slightly higher than rates of parent reported food allergy in the general population, it is a relatively small number compared to the number sensitized without clinical reactivity within this cohort. Thus, while approximately 1 in 8 siblings in this cohort was at risk of developing a food allergy, this number represents only a minimally increased potential risk over that of the general population (1 in 12). Given that 1 of 2 tested in this group was more likely to have clinically irrelevant sensitization, these data would suggest that screening of siblings would be inefficient and imprecise. This study therefore adds additional data to the confusing and evolving relationship between family history of food allergy within specific family members and the risk of development of food allergy in another family member.

Our findings help support the recommendations made in the current NIAID food allergy practice guidelines to not screen siblings prior to exposure to a food based on another primary sibling having a food allergy.² As has been a common experience, otherwise unselected children (including siblings of food allergic children) without a history of exposure to the particular allergen may often have food sensitization, but lack clinical reactivity to that food. Food sIgE and SPT in children who have not been exposed to an allergen result in a high rate of asymptomatic sensitization. This in turn may influence unwarranted food avoidance in the sensitized individual. Such unwarranted delayed introduction has recently been shown to increase the risk of developing peanut allergy in particular.³²

Previous studies exploring siblings of food allergic children included a cohort study in London where 7% of 34 siblings of reported peanut allergic children from a large cohort reacted to peanut on food challenge.¹⁸ A recent study of peanut, egg, and sesame allergy similarly found the prevalence of the aforementioned allergies among siblings of food allergic children to be 9.6%, compared to a prevalence of 5.6% among children without a food allergic sibling.²¹ In contrast to our findings, Liem et al concluded that siblings of peanut-allergic children are approximately 7-fold more likely to have reported peanut allergy than children in the general population (8.5% vs. 1.4%)¹⁹, though this study exclusively used survey methodology and did not actively verify sensitization in the entire cohort though reported sensitization levels were obtained from those self-identifying peanut allergy. Sicherer et al noted a similar rate of food allergy in siblings in a US survey, but without verifying sensitization.³³ Another study by Sicherer et al using a self-reported food allergy in a twin registry noted a 64.3% rate of concordance of food allergy among monozygotic twins studied.³¹ Unfortunately, the use of heterogeneous methodologies between our study and these other studies preclude any data pooling, and complicate comparison between

studies to better determine what the risk of sibling-to-sibling food allergy may be. With the exception of the Hourihane et al 1996 and Koplin et al 2013 data, no other studies used OFC, and in the Hourihane and Liem studies, there was not assessment in the siblings not reporting peanut allergy to assess the rate of asymptomatic sensitization. While our study utilizes parent reported food allergy status, to better validate this we stringently applied criteria of history and testing, determined by a physician panel.

The concern with potential screening and contextually asymptomatic sensitization tests in the sibling who has never eaten the allergen in question, is that many families defer having the child undergo a food challenge to confirm the allergy due to perceived risk of a reaction. In this sample, >50% of sensitized siblings would unnecessarily have avoided a food they could tolerate. Our rate of sensitization is similar to previously shown rates of 30% to 50%.^{35–37} Such a high rate of sensitization would lead to a higher rate of utilization of confirmatory OFC to rule in/out allergy. OFC is an expensive, time consuming and labor intensive clinical procedure. It has been long established that individuals may be asymptotically sensitized to foods, for a number of reasons, and thus sensitization alone is not sufficient to consider someone peanut allergic. These tests are sensitive, but not specific, accordingly, and allergy can be diagnosed only when there is a corroborating history of symptoms typical of an IgE mediated reaction attributable to ingesting that food. The limitations of such testing have been shown quite elegantly in NHANES data sets as well as in the Health Nuts study, where there are higher rates of sensitization than of possible or challenge proven allergy, in particular to peanut.

This study has several limitations. The data are nested from a cohort that started collection in 2008 and did not require that food allergy be confirmed via OFC. Proxy-reported food allergy status has an error rate in the accuracy of diagnosis relative to diagnosis made by OFC that is poorly quantified. While lack of verifying food allergy in our sample through the diagnostic gold standard of OFC is a weakness, conducting oral challenge for these children was not feasible. Indirect methods were used to assess the probability of a case representing true food allergy by integrating reported symptomatology with sensitization data to develop a stringent phenotypic definition. Similar approaches have been utilized in previous studies where investigators were unable to verify food allergy through the food challenge, and this is a readily accepted and valid research technique.^{22,24,33,38–41} An additional issue with this sample is that no comparison of rates were made in a replication cohort of non-allergic siblings, to compare the rate of allergy within siblings of allergic siblings compared to that in siblings of non-allergic siblings because the study only recruited families with food allergies. There are other limitations related to survey methodology. Data from proxy-reported allergy are subject to recall bias, as well as bias related to potential misperception of disease (e.g. what is and what is not an immunologic reaction to a food). Use of an enriched cohort of food allergic individuals also increases the potential for participation bias and selection bias. Lastly, this sample was comprised of predominantly white, upper-income married couples, and, as such, may poorly generalize to the US population.

In conclusion, only a small proportion of siblings were both sensitized and clinically reactive to a food. One third of siblings had no sensitization or clinical symptoms to a food and an

additional 53% were sensitized without clinical reactivity. Only 13% of siblings with evidence of food sensitization (sIgE or SPT) were allergic to the food, using a stringent grading criteria. Given the lack of a dramatically increased risk of food allergy in siblings compared to that of the general population, as well as the high rate of what are falsely positive diagnostic test results among siblings of a food allergic child, these data suggest siblings of food allergic children should not have routine screening for food allergy prior to food introduction. Such siblings are likely to be mislabeled as allergic when they are actually tolerant to the food, which may lead to an increased risk of developing allergy via avoidance. Such behavior may also adversely impact both quality of life and nutrition. Our data presented herein are consistent with current NIAID 2010 Food Allergy Guidelines and the 2015 JTFPP Food Allergy Practice Parameters and strengthen the current recommendations discouraging testing of siblings of food allergic children without a history of a symptomatic food ingestion.

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Abbreviations

IgE	Immunoglobulin E
sIgE	Allergen Specific Immunoglobulin E
SPT	Skin Prick Testing
kU/L	Kilo International Units per Liter
OFC	Oral Food Challenge

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What is already known about this topic?

Peanut allergy in one sibling may be a potential risk-factor for peanut allergy in the younger sibling, but little data are available about sibling-to-sibling risk of other allergies.

What does this article add to our knowledge?

The risk of clinically irrelevant food sensitization is several-fold more likely than sensitization with clinical reactivity, showing low frequency of sibling-associated risk of food allergy compared to falsely positive test results.

How does this study impact current management guidelines?

Food allergy screening of one sibling based on food allergy in another may be unwarranted, given a low prevalence of clinical reactivity and a high likelihood of detecting clinically irrelevant sensitization in siblings of food allergic children.

Table I

Demographic characteristics of participants.

	Frequency, %(n)	
	Index children (n=478)	Siblings (n=642)
Gender		
Male	63.6 (304)	48.1 (309)
Age, years		
0–1	5.7 (27)	18.2 (117)
2–5	50.0 (239)	40.2 (258)
6–10	32.6 (156)	30.1 (193)
11–13	9.2 (44)	6.9 (44)
14–20	2.5 (12)	4.7 (30)
Race/Ethnicity		
White	77.2 (369)	76.8 (493)
Black	4.0 (19)	4.5 (29)
Hispanic	9.0 (43)	10.1 (65)
Asian	2.1 (10)	1.9 (12)
Other	7.7 (37)	6.7 (43)
Household Income		
<\$ 50k	6.9 (33)	7.3 (47)
50–100k	28.2 (135)	29.4 (189)
>100k	63.0 (301)	61.4 (394)
Missing	1.9 (9)	1.9 (12)

Table II

Proportion of siblings who are sensitized to food

	Frequency, % (n)				
	Index child allergic to:				
	Any food (n=642)	Peanut (n=324)	Tree nut (n=132)	Milk (n=217)	Egg (n=155)
Sibling sensitized to:					
Any food	53.0 (340)	55.6 (180)	44.7 (59)	51.6 (112)	54.8 (85)
Peanut	24.6 (158)	22.8 (74)	28.0 (37)	23.5 (51)	31.6 (49)
Tree nut	16.7 (107)	16.4 (53)	21.2 (28)	15.2 (33)	21.3 (33)
Milk	35.4 (227)	37.4 (121)	38.6 (51)	27.2 (59) **	31.0 (48)
Egg	35.1 (225)	35.19 (114)	34.9 (46)	31.8 (69)	38.1 (59)
Soy	23.1 (148)	21.6 (70)	28.8 (38)	23.5 (51)	28.4 (44)
Wheat	36.5 (234)	36.7 (119)	43.2 (57)	33.6 (73)	37.4 (58)
Shellfish	14.8 (95)	14.8 (48)	18.2 (24)	11.5 (25)	15.5 (24)
Fish	3.9 (25)	4.3 (14)	6.1 (8)	3.2 (7)	2.6 (4)

Asterisks indicate statistical significance for association between sensitization and index child allergy.

* Indicates $p < 0.05$ ** Indicates $p < 0.01$

Table III

Proportion of siblings who have a clinical food allergy

	Frequency, % (n)				
	Index child allergic to:				
	Any food (n=642)	Peanut (n=324)	Tree nut (n=132)	Milk (n=217)	Egg (n=155)
Sibling allergic to:					
Any food	13.6 (87)	11.7 (38)	22.0 (29) **	12.9 (28)	17.4 (27)
Peanut	3.7 (24)	4.9 (16)	7.6 (10) **	1.8 (4)	3.9 (6)
Tree nut	1.6 (10)	1.5 (5)	2.3 (3)	0.9 (2)	0.7 (1)
Milk	5.9 (38)	4.0 (13) *	6.1 (8)	8.3 (18)	12.3 (19) **
Egg	4.4 (28)	4.9 (16)	8.3 (11) **	4.6 (10)	5.8 (9)
Soy	0.9 (6)	0.3 (1)	0.8 (1)	0.9 (2)	1.3 (2)
Wheat	1.1 (7)	0.9 (3)	0.0 (0)	1.4 (3)	2.6 (4)
Shellfish	0.2 (1)	0.0 (0)	0.8 (1)	0.0 (0)	0.0 (0)
Fish	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)

Asterisks indicate statistical significance for association between sibling clinical allergy and index child allergy.

* Indicates $p < 0.05$ ** Indicates $p < 0.01$

Table IV

Factors Predictive of Food Allergy or Food Sensitization

Variables	Food Allergy vs. None RRR (95% CI)	Sensitized vs. None RRR (95% CI)
Hygiene Factors		
Cold in first year	2.03 (0.88 – 4.67)	1.26 (0.79 – 2.02)
RSV in first year	1.01 (0.43 – 2.33)	0.86 (0.48 – 1.54)
Skin Infection	4.05 (0.72 – 22.60)	1.33 (0.24 – 7.26)
Eczema	3.60 (2.04 – 6.34) **	1.66 (1.12 – 2.45) *
Antibiotic use during first year	0.80 (0.44 – 1.45)	0.90 (0.62 – 1.32)
Asthma	4.14 (2.04 – 8.59) **	1.07 (0.62 – 1.86)
Age		
2–5	1.20 (0.52 – 2.74)	1.41 (0.87 – 2.31)
6–10	0.06 (0.32 – 2.01)	1.21 (0.72 – 2.02)
11–13	1.06 (0.30 – 3.81)	1.71 (0.74 – 3.94)
14–20	0.41 (0.10 – 1.73)	0.75 (0.30 – 1.88)
Race		
White	0.87 (0.43 – 1.77)	0.78 (0.50 – 1.23)
Gender		
Male	0.96 (0.56 – 1.66)	1.00 (0.69 – 1.44)
Household Income		
50–100K	2.59 (0.62 – 10.74)	1.32 (0.87 – 2.31)
>110K	4.59 (1.20 – 17.58) *	1.35 (0.68 – 2.67)
Missing	12.14 (2.25 – 65.42) **	0.69 (0.16 – 3.58)
Pets		
Dog	0.73 (0.36 – 1.48)	0.80 (0.52 – 1.24)
Cat	0.58 (0.23 – 1.47)	0.68 (0.40 – 1.14)
Family History		
Mother any atopy	1.45 (0.77 – 2.73)	1.16 (0.73 – 1.85)
Father any atopy	1.64 (0.87 – 3.10)	1.21 (0.82 – 1.80)
Number of siblings	1.19 (0.80 – 1.75)	1.27 (0.94 – 1.60)
Maternal Child Health		
Breastfeeding only	1.11 (0.58 – 2.13)	0.81 (0.53 – 1.26)
Childcare		
Home-based	0.73 (0.33 – 1.60)	1.13 (0.71 – 1.80)
Childcare center	0.83 (0.45 – 1.54)	0.89 (0.59 – 1.36)
Index child: Tree Nut Allergy		

Variables	Food Allergy vs. None RRR (95% CI)	Sensitized vs. None RRR (95% CI)
Tree Nut Allergy	1.99 (1.06 – 3.74) *	0.77 (0.47 – 1.25)

CI = 95% Confidence Interval

*
Indicates p<0.05

**
Indicates p<0.01