

The Prevalence of Food Allergies in Children Referred to a Multidisciplinary Feeding Program

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Abstract

Objective. To assess the prevalence of food allergy in children presenting to a multidisciplinary feeding program. **Methods.** A retrospective chart review was conducted from 302 patients. We recorded history of food reaction, family history of any atopic disease, radioallergosorbent testing, prematurity, birth weight, breastfeeding history, Z-scores, age, and gastrointestinal mucosal biopsy reports with eosinophilic infiltrate. Three categories of possible food allergy were stratified based on increasing evidence of allergy. **Results.** Possible food allergy was found for 18% (n = 54), likely food allergy for 6% (n = 18), and very likely food allergy for 16% (n = 47) for a total of 40% classified in a food allergy group. Having been breastfed correlated with likelihood of food allergy but tube-feeding dependence did not. **Conclusion.** This study revealed a higher proportion of children in a feeding program with food allergy compared to the general population, but larger prospective studies are needed to confirm the association.

Keywords

food allergy, atopy, childhood feeding disorder

Introduction

Feeding disorders in infants and young children occur in up to 25% of normal developing children and even more so in children with neurodevelopmental disorders.^{1,2} Food refusal (FR), gagging, and vomiting are common symptoms, whether the etiology to the feeding disorder is primarily due to behavioral or medical reasons. Unfortunately, even when the medical conditions have been treated and stabilized, infants and young children are still at risk for ongoing aversion to oral feeding. As a result of this potential nutritional compromise or undernutrition, there is a need for gastrostomy tube feeding to support the child's growth, which could interfere with advancement of oral feeding. Importantly, enteral access does not address feeding behaviors. Therefore, intensive multidisciplinary pediatric feeding programs composed of a team of therapists, psychologists, nurses, and physicians have become an established strategy for treating pediatric feeding disorders.^{3–5}

Medical diagnoses that have been associated with FR behaviors include gastroesophageal reflux disease (GERD), oropharyngeal dysphagia with swallowing

difficulties, placement of a gastrostomy tube in early infancy, cardiorespiratory disease, and neurologic disease.^{1,3,6} Although data are limited, food allergy has also been associated with feeding disorders in some studies.^{7,8} To further investigate the possible association of food allergy and feeding disorder in young children, we conducted a retrospective chart review from our multidisciplinary feeding disorders clinic to identify children with possible food allergy, stratifying them into groups with increasing evidence of food allergy. In addition, we compared each of these allergy categories to various patient characteristics including anthropometric data, prematurity, age at presentation for feeding program evaluation, and breastfeeding to identify potential predisposing factors.

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Materials and Methods

We conducted an institutional review board–approved retrospective chart review of all the patients evaluated at the Kennedy Krieger Institute Feeding and Swallowing Disorders Clinic from 1998 to 2003. Before admission into the day program, patients are first evaluated in the multidisciplinary clinic for feeding disorder because they are not feeding orally a normal diet for age and may have defensive behaviors surrounding feeding. Historical details that are usually elicited in the first evaluation clinic, and what was reviewed for the retrospective chart review, include past medical and surgical history, family history, medications, developmental, oral or tube feeding history, nutritional and growth histories. The types of medical diagnoses included prematurity, genetic syndrome, developmental disabilities, heart disease, chronic lung disease, and neurologic disease that interrupted normal feeding behavior as a young infant or toddler.

For the purposes of this retrospective study, data were collected when available from patient charts regarding a personal history of atopy, including eczema, allergic rhinitis, and asthma, as well as a family history of any atopic disease. In addition, radioallergen sorbent test (RAST) results, with a positive test defined as >0.35 kU/L, were collected for patients when they were available, as were food skin prick test results (positive = ≥ 3 -mm wheal). In addition, we collected available endoscopy and biopsy results. Biopsies in the esophagus are taken randomly at 2 to 3 levels, 2 biopsies each. Therefore, a total of 4 to 6 biopsies from at least 2 sites, the distal and middle esophagus, and from the stomach antrum and duodenum, usually 2 to 4 mucosal biopsies were obtained. It was not possible from this review to know which biopsies were performed through The Johns Hopkins Hospital since patients are referred from several outside institutions to the Kennedy Krieger Institute feeding program. Therefore, a final diagnosis of GERD, eosinophilic esophagitis (EoE), or eosinophilic gastroenteritis (EGE) disease was based on the pathologist's interpretation given on the biopsy report. This review included charts before the first consensus report defining EoE as greater than 15 eosinophils per high power field was available.⁹ Therefore, the early biopsies before 2002 interpreted as EoE were based on large numbers of eosinophils present on biopsy as was the practice at that time, but not recorded as a specific number per high power field. Since defined numbers are still not standard for a diagnosis of EGE, it was based on the pathologist's interpretation and report of an increased mucosal eosinophilic infiltrate on the biopsy of the duodenum and/or stomach.¹⁰ To be called GERD, biopsies may have a few

eosinophils, although less than 15 eosinophils per high power field, and pathologic criteria listed as "reactive epithelial changes" representing signs of gastroesophageal reflux in the esophagus.

We also documented birth history including gestational age, diet history, past medical history, and ethnic distribution as well as physical examination findings including weight, height, and Z-scores to compare results with the RAST testing, documented history of allergy signs, and biopsies with eosinophils. Data were entered into a secure database and tabulated for analyses.

We assigned definitions of allergy groups designed to sort out subjects with increasing evidence of allergy. Knowing that allergy diagnoses should not be based on RAST testing alone, we used the collective criteria of clinical data available as listed above from past medical and family history as well as RAST and biopsies with eosinophils when they were available. The groups were divided into possibly having food allergy, likely having food allergy, and very likely having food allergy. The "possible food allergy" group was defined as subjects who only had a report of a food reaction. We considered this the lowest correlation to food allergy because report of reaction may be unreliable. But precedence has been set in other reports of much larger studies including the National Health and Nutrition Examination Survey.^{11,12} The "likely food allergy" group was defined as subjects who had a reaction history and a confirmed positive RAST or skin-prick test of that food. The "very likely food allergy" group was defined as endoscopic evidence of EoE or EGE (primarily upper endoscopy) with or without positive skin/RAST testing or history of food reactions including anaphylaxis. Biopsies consisting of eosinophils infiltrated in the tissue in large numbers (greater than 15 eosinophils per high power field for the esophagus) and anaphylaxis to a food were considered examples that make food allergy highly likely (or definite with anaphylaxis) even if the RAST testing is not positive. The very likely food allergy group was the smallest group.

Statistical Analysis

In order to determine the sample size needed, an a priori power analysis was conducted using G*Power 3 software.¹³ For an independent-samples *t* test, the specified parameters included 2-tailed test, type 1 error probability of $\alpha = .05$, and power of .80. Based on these parameters, a sample size of 64 per group is required for a medium effect size of 0.50.

Spearman's rank order correlations were used to evaluate the relationship between patient characteristics (age at the time of the evaluation in months, gestational

Table 1. Likelihood of Food Allergy by Family History, History of Breastfeeding, and Tube Dependence^a.

	Change, M (SE)	95% CI	t (df)	P
Family history				
Eczema	-0.84 (0.30)	-1.47 to -0.21	-2.80 (19)	.011*
Food allergy	-1.28 (0.20)	-1.68 to -0.88	-6.48 (38)	.000*
Asthma	-0.48 (0.20)	-0.88 to -0.07	-2.33 (49)	.024*
Allergic rhinitis	-0.66 (0.20)	-1.06 to -0.25	-3.26 (52)	.002*
Any atopic	-0.66 (0.15)	-0.94 to -0.37	-4.50 (140)	.000*
Breastfed	-0.59 (0.15)	-0.88 to -0.29	-3.95 (162)	.000*
Tube dependence	0.03 (0.13)	-0.22 to 0.29	0.24 (290)	.808

Abbreviation: M, mean; SE, standard error; df, degrees of freedom; CI, confidence interval.

^aIndependent-samples *t* tests evaluated differences in participants based on likelihood of food allergy with family history, tube dependence, and history of being breastfed. The table provides mean differences and confidence intervals for mean changes.

**P* < .05.

age in weeks, height for age *z* score, weight for age *z* score, and birth weight in grams) with likelihood of food allergy. Independent-samples *t* tests were conducted to evaluate differences in participants based on likelihood of food allergy with family history, tube dependence, and history of being breastfed (Table 1). Chi-square analyses were conducted to examine endoscopy results for participants with negative or positive RAST results.

Results

A total of 302 charts were reviewed, including 130 females (42.9%) and 172 males (56.8%). The average age was 3.4 years (range = 4-159 months). The mean age of presentation with feeding concerns was 7.5 months (range = birth to 125 months; SD = 14.62), 103 had a history of prematurity, 106 a history GERD, and 141 had a gastrostomy tube at the time of admission.

Of these 302 children, 18% (*n* = 54) were categorized as possible food allergy, 6% (*n* = 18) were categorized as likely food allergy, and 16% (*n* = 47) were categorized as very likely food allergy. Therefore, overall, 40% of our population had at least possible food allergy and 22% had likely or very likely food allergy based on our more rigid criteria. The average number of suspected food allergies was 1 to 2 for those with a possible food allergy, 3 to 4 for those with likely food allergy, and 2 to 3 for patients with very likely food allergy. The most suspected food allergens included dairy (20%), soy (9.2%), egg (5%), peanut (3.6%), and wheat (3.6%). Breastfed infants had a higher likelihood of food allergy (*P* < .001), while tube feeding was not associated with having a food allergy (*P* = .808; Table 1).

Each of the food allergy groups were analyzed with regard to patient characteristics. No significant relationship regarding the likelihood of food allergy was found for age at evaluation in the feeding clinic (*r*_s[288] = -.10,

P = .090), gestational age (*r*_s[281] = .06, *P* = .312), height (*r*_s[266] = .06, *P* = .315), and weight (*r*_s[266] = .05, *P* = .379) Z-scores, or birth weight (*r*_s[255] = .09, *P* = .178). Instead, the only characteristics correlated with food allergy diagnosis were either a patient history or family history of atopic disease, in which a family history of asthma (*P* = .024), allergic rhinitis (*P* = .002), eczema (*P* = .011), food allergy (*P* < .001), or any atopic disease (*P* < 0.001) were all correlated.

With regard to suspected food reactions, symptoms included vomiting, diarrhea, eczema, urticaria, rash, irritability, edema, lethargy, abdominal pain, gas, itchy eyes/tongue, constipation, and respiratory distress. Symptoms of anaphylaxis (*n* = 4) and blood/mucus in stool (*n* = 6) were only reported in patients who fit the very likely category for food allergy in this report.

For those patients who had an endoscopy and RAST testing, we compared the presence or lack of eosinophilic disease, EoE or EGE, on the biopsies to the RAST results (Table 2). Our results using χ^2 analysis showed that having eosinophilic disease correlated with positive RAST test and did not with negative RAST test. On the other hand, as expected, the GERD diagnosis on pathology results had no relationship to RAST testing results.

Discussion

In this retrospective chart review from a pediatric feeding clinic, we found that up to 40% of patients had at least possible food allergy and that 22% had likely or very likely food allergy on presentation for evaluation to the clinic. This is the highest frequency of food allergy documented in the literature to date as a possible cause or contributor to FR. One explanation for this higher prevalence is that EoE was a newly reported diagnosis in 1995 thought to be a contributing factor to gastroesophageal reflux and feeding difficulties in children.¹⁴

Table 2. Endoscopy Results for Participants With Negative or Positive RAST Results and χ^2 and *P* Values^a.

	<i>F</i> (%)		χ^2 , <i>P</i> Value
	RAST Negative	RAST Positive	
Endoscopy			
Normal	6 (21.4)	0	
Abnormal	22 (78.6)	32 (100)	7.62, .006*
No GERD	15 (53.6)	19 (59.4)	
GERD	13 (46.4)	13 (40.6)	0.21, .651
No EO	23 (82.1)	9 (28.1)	
EO	5 (17.9)	23 (71.9)	17.51, .000*

Abbreviations: RAST, radioallergosorbent test; GERD, gastroesophageal reflux disease; EO, eosinophils.

^aThe table provides the frequency and percentage of participants with negative or positive RAST results and χ^2 and *P* values for endoscopy findings and breastfeeding history.

**P* < .05.

Therefore, diagnoses of EoE and food allergy became more consistently investigated at that time by the feeding group with documentation either by history or by objective data such as RAST testing, skin-prick testing, or endoscopy. However, the practice of ruling medical diagnoses including EoE and food allergy is still standard of care for patients presenting for evaluation to the intensive pediatric feeding program.

We also sought to determine whether any historical or physical characteristics were associated with food allergy. The only patient characteristics that we found associated with possible or likely food allergy were a family history of atopic disease or being breastfed. Furthermore, there was no association between being tube fed and being more likely to have food allergy in the feeding program.

We did find that a diagnosis of EoE was common in this population, which is consistent with another report that found 16.2% of children seen in a multidisciplinary eosinophilic gastrointestinal disorders clinic had a feeding disorder with FR behaviors, vomiting, and gagging.⁷ The other authors also found that some children in the feeding disorders group had persistent eosinophils present on esophageal biopsies. Our chart review, however, was not tailored for follow-up of the children with EoE to determine outcome since we reviewed the initial evaluation only. In fact, from a clinical standpoint we often see the opposite, that children may have persistent feeding issues even after the EoE has been effectively treated.

Levy et al¹⁵ found that cow milk protein allergy was diagnosed in 43% of the patients in a group they considered to have organic etiology to the FR behavior. However, they did not include data such as RAST or endoscopy testing or family history of atopy as we did. Interestingly, in our review, breastfeeding was associated with higher likelihood of food allergy. This could

be due to the fact that many of the food allergic children relied on breastfeeding for their major source of nutrition or that parents preferred to breast feed rather than to use hypoallergenic formulas.

Since this review is retrospective, it is limited by the amount of unavailable data. In addition, without double-blind food challenges the diagnosis of food allergy can never be certain and can be even harder to confirm in children with predominantly gastrointestinal symptoms related to food allergy. Therefore, we decided to categorize the patients into groups of “possible” versus “likely” versus “very likely” using data present in the chart that we determined would be indicators of food allergy. These conservative definitions could lead to some underestimation of true food allergy, but is preferred to being less strict, which can lead to marked overestimation.

Similarly, we considered pathologic diagnosis of EoE as an indicator of very likely food allergy. While not universally the case, the vast majority of young children with EoE are considered to have food allergy as the underlying etiology.¹⁶ EoE is a diagnosis made by histopathology. The pathologic diagnosis is made when the esophageal biopsy shows greater than 15 eosinophils per high power field. Clinically, it is considered to be due to a food allergy in most pediatric patients. The latest guidelines recommend initiating high-dose antacid therapy with proton pump inhibitor for 2 months prior to the endoscopy in suspected EoE cases in order to distinguish EoE from eosinophilic infiltrate on the esophageal biopsy that occurs with moderate to severe GERD.^{16,17} We did not have the specific definitions in the charts of this review because the charts originate before the first consensus guidelines were developed in 2007.¹⁸ Moreover, we used the pathologist’s interpretation of generally elevated numbers of eosinophils present anywhere in the gastrointestinal tract as indicator of very

likely food allergy. We could not use quantification of eosinophils other than in the esophagus because there is no standard quantification of eosinophils to diagnose eosinophilic disease in other locations throughout the gastrointestinal tract.^{19,20} Finally, a significant limitation of this review is that we only had access to the biopsy report and were not able to review the slides to confirm the degree of eosinophilic infiltrate.

The true prevalence of food allergy in children overall has been shown to be between 1% and 10% in a variety of studies and populations.^{11,12,21} In 2011, Gupta et al¹² reported on the largest population, reaching out to over 40000 US households of English- and Spanish-speaking families, determining US prevalence of food allergy to be 8%. Multiple food allergies occurred in 2.4% of children. Of note, as we used parent report for food allergy history, so did these reports, which are considered benchmark data. As our study is a retrospective chart review with incomplete data, we are not able to make definitive conclusions about the true incidence of food allergy in this population, although there is little doubt that it is far higher than the general population.

An important question with regard to the relationship of food allergy to feeding disorders is whether identifying food allergies earlier could potentially prevent future feeding difficulties. While we cannot answer this question with these data, we would encourage that any medical condition that may lead to feeding disorders, whether it be GERD or food allergy, be addressed promptly when concerns arise. This equation is limited, however, by the difficulty in diagnosing food allergy, especially in infants and even more so in those with predominantly gastrointestinal symptoms.

In conclusion, this study from a large database evaluating children who presented for an initial pediatric feeding evaluation revealed a far higher proportion with food allergy compared to the general population. Z-scores for weight and height, gestational age, birth weight, tube feeding, and age of presentation to the feeding program did not predict food allergy in this population. While these data strongly suggest that food allergy may be an important factor leading to feeding disorders, prospective studies with larger populations will be needed to clarify the true relationship of food allergy to feeding disorders, ideally with long-term follow-up to discern benefits of food allergen avoidance in those with a confirmed diagnosis of food allergy.

Author Contributions

KAU: paper composition and study design; TT: statistical analysis, paper composition, and study design; AS: study design, data collection/chart review, and paper composition; RC: study design, data collection/chart review, and paper

contribution; ER: data collection, paper contribution; PG: study design, paper contribution; RW: study design, statistical analysis, and paper composition.

Declaration of Conflicting Interests

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