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Degree of Anxiety in Food Allergic Children in a Tertiary Care Center

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Keywords

Food allergy; anxiety; atopic disorders; psychiatry; pediatrics

Introduction

Atopic diseases, including asthma, allergic rhinoconjunctivitis, atopic dermatitis, and food allergy, are the most common chronic medical conditions that affect children and adolescents. In the United States, the estimated prevalence of asthma in children is 8-10%, the estimated prevalence of allergic rhinitis is 8.5-14.6%, and the estimated prevalence of food allergy is 4-8%^{1, 2, 3, 4}. Most children with atopic disease develop symptoms prior to six years of age^{5, 6, 7}. Similarly, anxiety disorders occur frequently in children and adolescents, with an estimated lifetime prevalence of 31.9%⁸, and many children will develop symptoms when they are quite young; the median age of onset anxiety disorders is

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six years old⁸. It is crucial to detect anxiety disorders early since untreated anxiety symptoms may lead to negative downstream effects including poor school attendance, impaired development of social skills, higher risk for additional mental health problems, and higher risk for substance abuse⁹. Anxiety disorders are more common among children with medical illnesses^{10, 11, 12, 13}; the combination leads to increased medical and psychiatric morbidity in adulthood¹⁴. Children with comorbid anxiety disorders and medical illnesses have a high risk of developing mental health problems as adults. These findings, along with the high prevalence of allergic diseases and anxiety disorders among children, have led to a heightened interest in the comorbidity between these two conditions.

Multiple studies have shown that food allergy has a negative impact on the quality of life (QoL) for both food allergic children and their parents; and many look at the role anxiety plays^{15, 16, 17, 18}. The fear of accidental exposure to food allergens, the need to carry medication at all times, and the potential limitations on social activities could be sources of anxiety for food allergic children and their parents. In a study of children with peanut allergy, those with a history of needing to inject epinephrine and having parents who reported higher stress scores, reported higher anxiety levels than children with peanut allergy who did not have these other factors¹⁷. LeBovidge and colleagues found that mothers of children with food allergy reported more symptoms of anxiety and depression in their children compared to data from a normative sample of children. However, the children themselves did not report increased anxiety compared to 56 age-appropriate normative samples (mean age, 8.3 years)¹⁸. In addition, 86 young adults with self-reported food allergy (mean age, 20.8 years) did not have increased levels of anxiety as compared to 334 unaffected peers (mean age, 20.8 years)⁷.

In an adult German general population sample of over 4,000 people aged 18-65, self-reported allergic disease was associated with an increased likelihood of having a mood or anxiety disorder. Additionally, in this cohort, self-reported allergy was associated with an increased likelihood for several specific psychiatric diagnoses including panic attacks, panic disorder, generalized anxiety disorder, specific phobias, major depressive disorder, and bipolar disorder¹⁹. Other findings suggest that the relationship between atopic disease and psychiatric illness is specific to anxiety disorders. In a study of 343 children and adolescent anxiety patients (mean age, 11.6 years), allergy symptoms were more common among those with separation anxiety disorder, but not among those with other anxiety or psychiatric disorders²⁰. Similarly, 184 children and adolescents in a slightly smaller, older group (mean age, 13.2 years) diagnosed with an internalizing disorder, such as anxiety and/or depression, had a higher frequency of allergy symptoms than those diagnosed with non-internalizing disorders²¹. A study of 477 school-aged children in Australia (mean age, 9.0 years) showed that those with asthma had substantially higher levels of anxiety as compared to those without asthma²².

The data on food allergy and its association with anxiety disorders are inconsistent; however, this may be due to methodological differences within the aforementioned studies. There is a wide range of sample sizes across the studies^{7, 16, 17, 18, 19, 20, 21}. Instruments used to assess anxiety also varied; some studies utilized an established scale designed to measure anxiety

and other psychiatric issues^{15, 17, 19, 20}, while others relied on invalidated QoL instruments and self-reported anxiety symptoms through interviews and surveys^{16, 21, 23}.

The above review reinforces the notion of inconsistent results regarding the prevalence of anxiety disorders within children with food allergies. The current study aims to further explore this relationship within a diverse sample of children and adolescents. A group of children with an allergist-confirmed food allergy and a group of children with an anxiety disorder were compared to children from a general pediatric clinic, seen during well-child exams, who served as our control group. It was hypothesized that children with confirmed food allergies would score significantly higher on a standardized anxiety screen than children from the general pediatric clinic, but would not score as high as children with a confirmed anxiety disorder.

Methods

Participants

This study was approved by the Institutional Review Boards of the Penn State Milton S. Hershey Medical Center and Penn State College of Medicine. Participants were patients from one of three outpatient clinics at the Penn State Milton S. Hershey Medical Center (HMC): the Penn State Hershey Children's Hospital Allergy & Immunology Clinic (ALG), the Anxiety Disorders Clinic at the Outpatient Psychiatry Clinic (ANX), and the General Pediatrics Clinic (GP). Patients were eligible for the study if they were between the ages of 8 and 16 and had a confirmed food allergy diagnosis, or a confirmed anxiety disorder diagnosis, or were being seen for a well-child visit. Food allergy was confirmed by a pediatric allergist based on clinical history and through results of skin testing, serum IgE testing, and/or in-office oral challenge.

The diagnosis of an anxiety disorder was determined by clinical interview by a child and adolescent psychiatrists or psychologists. Patients were diagnosed with anxiety disorders based on Diagnostic and Statistical Manual of Mental Disorders IV-TR criteria. Study groups included 37 children within the ANX group (mean age, 12.7 years), 38 children within the ALG group (mean age, 11.8 years), and 39 children within the GP group (mean age, 12.5 years). It was estimated that a sample size of 36 individuals with FA would produce 80% probability of a 20% increase of any anxiety disorder with a 5% type I error.

Procedures

Study visits were conducted in person by the investigators. On recruitment days, the physician or psychologist-investigator, along with a research technician, reviewed the appointment list to identify patients eligible for participation in the study. At the general pediatric control site, all children coming for a well-child exam were offered participation if they met inclusion criteria. At the anxiety control site, on the day of the recruitment all children with a diagnosis of anxiety coming for a follow up by the child psychiatrist or psychologist were offered participation if they met inclusion criteria. At the allergy control site, on the day of the recruitment, all children with a diagnosis of food allergy coming for a follow by pediatric allergist were offered participation if they met inclusion criteria.

At all three sites, patients and their parent(s) who provided written consent to participate completed all measures necessary for the study. Percentages were not recorded, but a majority of patients that were asked agreed to be in the study; the most common reason for not participating was due to time constraints. Children completed measures asking them to self-report their anxious and allergic symptoms; similarly, parents also rated their child's symptoms on parent-reported forms. Study data were collected and managed using REDCap (Research Electronic Data Capture), a secure, web-based application designed to support data capture for research studies²⁴.

Measures

Screen for Child Anxiety Related Emotional Disorders (SCARED)—The SCARED is a 41-item standardized screen for anxiety validated for use in children ages 8-16²⁵, and also features a parent-report form. The child version, or self-report form, is answered by the child in regards to their own anxiety. The parent-reported SCARED form is completed by parents, as they answer questions in regards to their child's anxiety. Responses to the items are summed to create a composite score and scores on individual subscales. A composite score of 25 or greater suggests the presence of an anxiety disorder, along with clinical cut-off scores for each of the five subscales (Panic Disorder, Generalized Anxiety Disorder [GAD], Separation Anxiety, Social Anxiety, and School Avoidance). It has demonstrated acceptable reliability and validity²⁶. Patients from all three groups (ALG, ANX, GP) completed the self-report SCARED. One or both parents/guardians accompanying the child completed the parent-report SCARED.

Food Allergy Questionnaire—The Food Allergy Questionnaire (FAQ) is a non-standardized, physician-designed instrument used to assess various areas of a patient's allergy background, including evaluation, treatment, diagnosis, and familial allergy history. This 22-item self-reported questionnaire is designed with seven headings that ask about food allergies, eczema, asthma, and other allergic diseases within the ANX and GP groups. Patients also reported whether they have experienced symptoms of an allergic reaction (e.g., itching in the mouth, tightening of the throat) after contact with certain foods and the characteristics of their allergic reaction if they reported a food allergy. If a patient reported a food allergy, they also indicated whether they believed their allergies were related to their anxiety. Parents were instructed to assist in filling out questionnaires for participants less than 14 years-old.

Anxiety Disorder Questionnaire—This investigator-designed questionnaire inquires to the patient's and parent's history of anxiety disorders and obsessive compulsive disorder within the ALG and GP groups. If the patient or parent reported a disorder, they reported any treatment that they have received. Patients self-reported whether they believed their allergies and anxiety to be related, and if they believed their parents to be anxious. Parents indicated whether they believed their child's anxiety and allergy were related, and whether their anxiety related to their child's allergy. Parents were instructed to assist in filling out questionnaires for participants less than 14 years-old.

Medical Chart Review—A medical chart review was conducted by a member of the study team to support any self-reported diagnoses collected on the Food Allergy Questionnaire (FAQ) and the Anxiety Disorder Questionnaire. Responses to the FAQ and medical chart data were reviewed by the allergist on the study team to establish a probable food allergy diagnosis in ANX and GP patients. Asthma, eczema, medication allergy, and anxiety disorder diagnoses reported on the questionnaires were corroborated by reviewing the patients' medical records. In cases of disagreement, we deferred to the medical record data.

Statistical Analyses—In order to compare composite and subscale scores derived from the self and parent-report SCARED among the ALG, ANX, and GP groups, a one-way analyses of variance (ANOVA) was utilized, followed by a post-hoc trend analysis. Chi-square tests examined differences in: 1) the rates of food allergies, asthma, and eczema within the ANX and GP patients; and 2) the rates of elevated scores on the SCARED across the three groups.

Results

Demographics

Differences in demographics are presented in Table 1. There was no significant difference in age, but there were significant differences in gender across the three groups. There was a higher number of boys seen in the ALG group ($N = 29$, $p = 0.027$) when compared to the ANX and GP groups ($N = 19$ in both groups). In addition, no significant differences were detected in the incidence of allergic diseases in the ANX or GP groups. These rates were reported within questionnaires but were not confirmed by an allergist (Table 2).

Self-Report SCARED

After adjusting for age and gender, significant overall differences were observed among the three groups on majority of the self-reported SCARED scales (Table 3). Results from the post-hoc trend analysis, however, did not demonstrate any significant trends on any of the self-reported subscales. Alternative analyses utilized chi-squares to view differences in the number of children surpassing the clinical threshold across the three groups on the self-report SCARED. Overall significant differences between the three groups were detected on half of the subscales (Table 4). A 2×2 chi-square did not observe any significant differences between the ALG and GP groups, however.

Parent-Reported SCARED

One-hundred and eight mothers, 10 fathers, and for four children, both parents completed the parent version of the SCARED form about their child's anxiety. Initial analyses focused on mother-reported SCARED forms due to the lack of data from the majority of fathers. After adjusting for age and gender, results demonstrated significant overall differences among the three groups on all of the mother-reported SCARED subscales (Table 3). Post-hoc trend analyses demonstrated a trend within the Panic Disorder subscale, but this did not reach statistical significance ($p = 0.071$) (Figure 1). A sensitivity analysis was repeated by adding the 10 father cases to create a larger sample. Analyses were repeated with the additional cases, but observed no significant trends on any of the scales.

Chi-squares were utilized to view the number of children scoring in the clinical threshold across the three groups on the mother-reported SCARED. Results demonstrated significant overall differences among the three groups on majority of the scales (Table 4). Differences between the ALG and GP groups were analyzed with 2×2 chi-square; results demonstrated no significant differences between the two groups. Chi-square analyses were repeated on the larger mother-father sample and yielded the same findings. There were significant differences among the three groups on majority of the scales, yet a 2×2 chi-square found no significant differences between the ALG and GP groups.

Discussion

To the best of our knowledge, this is the first study to compare a group of children with food allergy to both children with known anxiety disorders and a healthy control group from a general pediatric clinic. The ALG group appeared to be very similar to the GP control group on both forms of the SCARED, and did not show evidence for increased anxiety. Trend analyses suggested a trend for mothers of children in the ALG group to report more panic disorder symptoms in their children, but this finding was not significant. By using a validated anxiety screening tool (e.g., SCARED) to compare the three groups instead of comparing to normative data, we were able to get a better understanding of the levels of anxiety in our local population. Our results are consistent with other studies showing that children with food allergies do not appear to have increased levels of anxiety. One hypothesis for the lack of increase in anxiety measure is that the children have solid cognitive and emotional mechanisms for coping. Another possibility is that the recruits were resilient in regards to their personality traits as seen on their SCARED scores.

This study has several limitations. Our data are cross-sectional; all children who met inclusion criteria on the day of the recruitment were offered participation, but children were at different stages of their medical or mental health treatments. For the ALG group, it is possible that there is an increase in the anxiety level in children following a new diagnosis of food allergy compared to anxiety levels in established patients who have been managing their food allergy for longer periods of time. Previous studies have shown that older food allergic children and their mothers have improved allergy-specific QoL scores, possibly because they have adjusted to living with their food allergy^{19, 27}. Also, we did not document the severity of previous allergic reactions; children with a history of more severe reactions may have more anxiety as compared to those with less severe reactions²⁸.

Lastly, family coping patterns may play a role in anxiety as some families may be more resilient than others. A recent study looked at patterns of adaptation in a group of food allergic children and their parents and found that families can be clustered into groups based on their anxiety traits and their food allergy competence. Those who had a “balanced response” were able to incorporate food allergy into their daily life without increased levels of anxiety²⁹; the other groups may benefit from a referral for behavioral health services.

As expected, SCARED scores were highest at this site since all of the ANX children were currently undergoing anxiety treatment. We did not screen participants to see how long they had their anxiety diagnosis. The sample had a higher rate of males in the ALG group as

compared to ANX and GP groups, which is consistent with the literature that shows the rates of food allergy higher in boys as compared to girls³⁰. However, anxiety is more often seen in females³¹, thus potentially reducing the number of children with anxiety in the ALG group. This study assessed children age 8-16 at the food allergy clinic and there was no assessment of younger children. Parental or child anxiety screens may show different levels of anxiety if assessed at younger ages, immediately after the diagnosis, or within the year of confirmed diagnosis. Since most food allergies are diagnosed by six years of age, anxiety levels may be higher in younger children. This is an area of potential study.

Our sample was primarily Caucasian, which reflects the demographics of our recruitment area. In addition, there was a paucity of collected data from fathers, which is simply because few fathers were present at their child's appointment. This may have improved if we had a larger sample size. Although secondary analyses did include father data, the majority of the data analyses were conducted using only mother data. This was done due to evidence suggesting that gender plays a role in coping with food allergies³¹. Gender may be evident through parental reports; a study looking at children and adolescents with food allergies found that mothers reported increased levels of anxiety, depression, and ADHD within their children when compared to their child's self-report³². Our findings highlight how mothers report on their child's anxiety symptoms, not on their own symptoms. However, this may have influenced their reports which lead to the trend in panic disorder symptoms, and is a potential area of further study.

Food allergy is a significant health issue with a potential for both morbidity and mortality. The association with anxiety disorders, although inconsistent, still remains an important clinical concern. Many factors can influence this association, and it is critical to remember that this diagnosis affects both the child and the parent. Keeping in mind that food allergy can cause life-threatening reactions; children and parents still may struggle with this diagnosis. The use of an anxiety screening tool, such as the SCARED, in allergy clinics may be very useful in objectively screening for anxiety symptoms in children with food allergies. Those with higher scores may benefit from further mental health referral. While it continues to be important to screen food allergic children for anxiety symptoms and refer for mental health services when indicated, it is encouraging that in our study population, children with food allergy did not appear to have increased anxiety as compared to a healthy control group.

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Appendix

Author Contributions:

Lidija Petrovic-Dovat M.D.: Dr. Petrovic – Dovat approved the final version of the manuscript. She is the Principal Investigator, and first and corresponding author, for this study. Her contributions toward this study include conception and design of the study, data generation, analysis and interpretation of the data, and preparation and critical revision of the manuscript.

Tracy B. Fausnight, M.D.: Dr. Fausnight approved the final version of the manuscript. She shares first authorship with Dr. Petrovic-Dovat. Her contributions toward this study include conception and design of the study; data generation, analysis and interpretation of the data, and preparation and critical revision of the manuscript.

Amanda White, B.S.: Ms. White approved the final version of the manuscript. Her contributions towards this study include data generation, analysis and interpretation of the data, and preparation and critical revision of the manuscript.

Timothy Zeiger, PsyD: Dr. Zeiger approved final version of the manuscript. His contributions towards this study include overall conception and design of the study. In addition, he assisted in conducting literature reviews, participant recruitment, data generation, analysis and interpretation of the data, and preparation and critical revision of the manuscript, including review of various drafts of the initial abstract.

Pevitr S. Bansal, M.S.: Mr. Bansal approved the final version of the manuscript. His contributions towards this study include data generation, analysis and interpretation of the data, and preparation and critical revision of the manuscript.

Nidhi Garg, M.D.: Dr. Garg approved the final version of the manuscript. Her contributions towards this study include conception and design of the study, data generation (when applicable), and preparation or critical revision of the manuscript.

Jitendra Annapareddy, M.D.: Dr. Annapareddy approved the final version of the manuscript. His contributions towards this study include conception and design of the study; analysis and interpretation of the data, and preparation or critical revision of the manuscript.

Sarah Iriana, M.D.: Dr. Iriana approved the final version of the manuscript. Her contributions towards this study include data generation, analysis and interpretation of the data, and preparation or critical revision of the manuscript.

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Edward O. Bixler, PhD: Dr. Bixler approved the final version of the manuscript. His contributions towards this study include conception and design of the study, analysis and interpretation of the data, and preparation and critical revision of the manuscript.

Marisa Klein, B.S.: Ms. Klein agreed to be mentioned in the acknowledgement section of the manuscript. She contributed to the conception and design, along with overall administrative support for the study.

Abbreviations:

FA (Food Allergy)

Immune system reaction occurring soon after eating a food

ANX (Anxiety)

Children presenting with mental health issues congruent with anxiety

ALG (Allergy)

Children presenting with medical issues congruent with allergies

GP (General Pediatrics)

A group of children receiving a well-child check-up exam

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Figure 1.
Maternal-Reported Panic Disorder Symptoms

Table 1.

Demographic Characteristics and Group Differences

	ANX	ALG	GP	Sig.
Age (M ± SD)	12.7 ± 2.1	11.8 ± 2.3	12.5 ± 2.7	.373
Male N (%)	19 (51.4%)	29 (72.5%)	19 (44.2%)	.027*
White/Caucasian N (%)	34 (91.9%)	34 (85%)	37 (86%)	.624

Table 2.

Patient and Parent-Reported Allergic Disorder Rates within Anxiety and General Pediatric Clinics

		ANX N (%)	GP N (%)	<i>p</i>
Asthma	Yes	11 (29.7)	7 (16.3)	0.15
	No	26 (70.3)	36 (83.7)	
Eczema	Yes	7 (18.9)	7 (16.3)	0.76
	No	30 (81.1)	36 (83.7)	
Food Allergy	Yes	5 (13.9)	3 (7.0)	0.31
	No	31 (86.1)	40 (93.0)	

Table 3.

SCARED Total and Subscale Scores by Research Site

	CHILD					MOTHER				
	Adjusted Means*					Adjusted Means*				
	ANX	ALG	GP	Overall	<i>p</i>	ANX	ALG	GP	Overall	<i>p</i>
Total	M ± SD	M ± SD	M ± SD	M ± SD	Overall	M ± SD	M ± SD	M ± SD	Overall	ALG vs. GP
	31.2 ± 2.2	18.3 ± 2.2	19.9 ± 2.2	< 0.001	0.309	28.8 ± 2.0	14.2 ± 2.1	13.0 ± 2.0	< 0.001	0.929
Panic Disorder	6.7 ± 0.7	3.3 ± 0.7	3.9 ± 0.7	0.002	0.327	5.1 ± 0.6	2.6 ± 0.6	1.0 ± 0.6	< 0.001	0.126
GAD	8.8 ± 0.6	5.0 ± 0.6	5.3 ± 0.6	< 0.001	0.257	9.3 ± 0.7	4.6 ± 0.7	4.8 ± 0.7	< 0.001	0.572
Separation Anxiety	6.0 ± 0.5	3.3 ± 0.5	3.7 ± 0.5	< 0.001	0.452	5.0 ± 0.6	1.8 ± 0.6	2.4 ± 0.6	0.001	0.541
Social Anxiety	7.3 ± 0.6	5.4 ± 0.6	5.5 ± 0.6	0.158	0.815	6.6 ± 0.6	4.3 ± 0.6	4.0 ± 0.6	0.024	0.893
School Avoidance	2.4 ± 0.3	1.3 ± 0.3	1.5 ± 0.3	0.015	0.456	2.9 ± 0.3	0.9 ± 0.3	0.8 ± 0.3	< 0.001	0.961

* Adjusted for Age & Gender

Table 4.

Comparison of SCARED Scores Surpassing Clinical Threshold

	CHILD					MOTHER				
	ANX	ALG	GP	Overall	<i>p</i>	ANX	ALG	GP	Overall	<i>p</i>
	N (%)	N (%)	N (%)			N (%)	N (%)	N (%)		ALG vs. GP
Total	23 (52.3)	9 (20.5)	12 (27.3)	0.001	0.485	22 (68.8)	6 (18.8)	4 (12.5)	<0.001	0.405
Panic Disorder	12 (48.0)	5 (20.0)	8 (32.0)	0.126	0.389	12 (80)	2 (13.3)	1 (6.7)	<0.001	0.504
GAD	21 (61.8)	6 (17.6)	7 (20.6)	<0.001	0.800	20 (64.5)	6 (19.4)	5 (16.1)	<0.001	0.627
Separation Anxiety	22 (48.9)	14 (31.1)	9 (20.0)	0.005	0.187	13 (52.0)	5 (20.0)	7 (28.0)	0.077	0.638
Social Anxiety	16 (39.0)	14 (34.1)	11 (26.8)	0.390	0.418	12 (54.5)	6 (27.3)	4 (18.2)	0.051	0.405
School Avoidance	14 (50.0)	6 (21.4)	8 (28.6)	0.066	0.591	18 (78.3)	3 (13.0)	2 (8.7)	<0.001	0.572