

Original Article

The Psychosocial Impact of Food Protein-Induced Enterocolitis Syndrome

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What is already known about this topic? Food protein–induced enterocolitis syndrome (FPIES) is a non-IgE, cell-mediated food allergy. Despite recent advances in understanding medical aspects of the condition, little is known about its psychosocial impact.

What does this article add to our knowledge? There is a high degree of psychosocial burden among caregivers of children with FPIES. Caregivers with lower income, affected children avoiding multiple foods, or avoiding cow's milk are at higher risk.

How does this study impact current management guidelines? Children with FPIES and their caregivers have increased psychosocial stress. Additional research into the psychosocial impact of FPIES is needed to develop practical interventions to better support families.

BACKGROUND: Little is known about the psychosocial impact of food protein–induced enterocolitis syndrome (FPIES).

OBJECTIVE: To characterize quality of life, stress, worry, anxiety, and self-efficacy in caregivers of children with FPIES and affected children, and determine risk factors for increased psychosocial burden.

METHODS: Surveys completed by caregiver-members of the International FPIES Association at a conference ($n = 42$) and online ($n = 368$) were analyzed.

RESULTS: There was significant burden, stress, worry, and anxiety among caregivers. There was a positive correlation among Food Allergy Quality of Life-Parental Burden, Perceived Stress Scale-10, Penn State Worry Questionnaire, and Beck Anxiety Inventory scores, and these were negatively associated with Food Allergy Self-Efficacy for Parents (FASE-P) scores. Lower income was associated with poorer caregiver health-

related quality of life (HRQoL) ($P = .039$) and lower FASE-P ($P = .028$). Greater number of food groups avoided correlated moderately with poorer HRQoL ($r = 0.386$; $P < .001$), higher anxiety among preschoolers ($r = 0.262$; $P = .013$) and parents ($r = 0.594$, $P = .025$). Avoiding cow's milk due to FPIES was associated with poorer caregiver HRQoL ($P < .001$), higher stress ($P = .001$), and lower FASE-P ($P = .013$). Caregivers whose child was not attending daycare/school due to FPIES had poorer HRQoL ($P < .001$), higher stress ($P < .014$), and worry ($P = .004$). Compared with published cohorts of caregivers of children with IgE-mediated food allergy, the burden of FPIES on caregivers was significantly higher (mean = 3.4 vs 3.0; $P < .001$) and self-efficacy was significantly lower (mean = 63.9 vs 76.1; $P < .001$).

CONCLUSIONS: There is increased stress, worry, anxiety, and reduced HRQoL and self-efficacy among caregivers of children

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*Abbreviations used**ED- Emergency department**FA- Food allergy**FAQL-PB- Food Allergy Quality of Life-Parental Burden**FASE-P- Food Allergy Self-Efficacy for Parents**FPIES- Food protein–induced enterocolitis syndrome**GAD- Generalized anxiety disorder**HRQoL- Health-related quality of life**I-FPIES- International FPIES Association**OCD- Obsessive-compulsive disorder**PSS-10- Parent Perceived Stress Scale-10**PSWQ- Penn State Worry Questionnaire**SCAS- Spence Child Anxiety Scale**SCAS-P- Spence Child Anxiety Scale for Parents**SD- Standard deviation*

with FPIES and increased general anxiety among pre-schoolers. Additional research is needed to inform effective psychosocial interventions. © 2020 American Academy of Allergy, Asthma & Immunology (J Allergy Clin Immunol Pract 2020;■:■-■)

Key words: Food protein–induced enterocolitis syndrome; Non–IgE-mediated; Food allergy; Pediatric; Psychosocial; Stress; Anxiety; Worry; Self-efficacy; Quality of life

Food protein–induced enterocolitis syndrome (FPIES) is a non–IgE-mediated food allergy (FA) that presents with gastrointestinal symptoms and occurs in both acute and chronic forms. Although FPIES has been described as “rare,”¹ recent population-based data indicate that it is not.^{2,3} In 2019 in the United States, FPIES was reported to affect 0.5% of the pediatric population and 0.2% of the adult population.³ Despite this prevalence, many medical providers are unfamiliar with FPIES. Symptoms of FPIES may be confused with infectious enteritis in mild-to-moderate cases and sepsis in severe cases.⁴ Attempts have been made to raise awareness of this disorder among the medical community, yet some families are still unable to find a physician experienced in this area.⁵ The first guidelines addressing diagnosis and management of FPIES were published in 2017 and provided consensus guidance for diagnosis and treatment; however, FPIES remains a clinical diagnosis.⁶ These factors often lead to delayed diagnosis or misdiagnosis, which can lead to anxiety regarding food introduction among caregivers of children with FPIES.

There is limited information on the psychosocial impact of FPIES on patients and caregivers.^{5,7,8} To our knowledge, there are only 2 published articles examining health-related quality of life (HRQoL) related to FPIES. The first article by Schultz and Westcott-Chavez⁵ is written from a parent’s perspective and serves as a call for better recognition and understanding of FPIES in the medical community while simultaneously raising awareness of the emotional burden faced by families. The second article by Greenhawt et al⁸ compares HRQoL in caregivers of children with FPIES with that of caregivers of children with IgE-mediated FA. Using the validated Food Allergy Quality of Life-Parental Burden (FAQL-PB) questionnaire, they found that caregivers of children with FPIES had worse HRQoL than caregivers of children with IgE-mediated FA on both individual domains and mean total score.⁸ Notably, the mean total

difference between these 2 groups was almost 3 times greater than the FAQL-PB’s minimum clinically significant difference in the FPIES cohort, suggesting a strikingly greater impact of FPIES on caregiver HRQoL than IgE-mediated FA.⁸

There remains a need to better characterize the social and emotional burdens of living with FPIES and its effect on HRQoL among caregivers and children. The goal of this study was to characterize HRQoL, stress, worry, and anxiety among caregivers and affected children recruited from a geographically diverse population. We hypothesized that lower income, greater number of food groups avoided, more than 1 child with FPIES, caregiver-reported anxiety/depression, and keeping a child out of daycare/school due to FPIES would be associated with poorer HRQoL, greater stress, worry, and anxiety, and lower FA-related self-efficacy.

METHODS

Design

The Boston Children’s Hospital Institutional Review Board approved this study. Surveys (Figure E1, available in this article’s Online Repository at www.jaci-inpractice.org) were completed electively by caregivers who self-identified as having a child diagnosed with FPIES and their affected children. Participants were recruited from (1) an FPIES Education Conference held on August 4, 2018, in Philadelphia, PA (n = 42 of 95 distributed surveys; response rate 44.2%), and (2) the International FPIES Association (I-FPIES) website and Facebook page between December 3, 2018, and January 7, 2019 (n = 368 of 5183 I-FPIES caregiver-members; response rate: 7.1%). I-FPIES is a recognized 501(c)3 nonprofit organization that provides education and advocacy for individuals with FPIES and their families, with chapters in Australia, Austria, Brazil, Egypt, Germany, Italy, the United Kingdom, the United States, and Qatar. Approximately 72% of 5183 members are in the United States. The exact location of survey respondents could not be determined for this study. To ensure that the children represented were not counted twice in the analysis, surveys completed at the conference by multiple caregivers within the same family were marked and subjects completing surveys online were instructed to complete 1 survey per family.

Measures

Demographic and Medical Questionnaire. Caregiver demographics were obtained, including age, sex, race, marital status, household income, education level, and other medical comorbidities (Figure E1, available in this article’s Online Repository at www.jaci-inpractice.org). The survey asked the caregiver to report medical conditions of anxiety or depression but did not query if these conditions were physician-diagnosed. Demographic data for all children in the family with FPIES, including age, sex, race, atopic comorbidities, and daycare/school attendance, were also obtained. Families self-reported which foods were avoided due to FPIES. Foods were divided into 13 “groups”: cow’s milk, soy, egg, peanut, tree nuts, fishes, shellfishes, poultries, meats, grains, vegetables, fruits, and other. We did not have access to medical records to confirm physician diagnosis of FPIES or determine whether oral food challenges had been performed.

Food Allergy Quality of Life-Parental Burden. The FAQL-PB is a 17-item questionnaire designed to capture caregiver HRQoL in children aged 0–12 years with FA. Items are rated on a 7-point Likert scale (0 = not limited/troubled to 6 = extremely

limited/troubled); a mean score is calculated with higher scores indicating poorer HRQoL. The FAQL-PB has been previously validated in an IgE-mediated FA cohort⁹ and in patients with FPIES.⁸ The measure exhibited excellent internal consistency in our sample (Cronbach's $\alpha = 0.95$).

Parent Perceived Stress Scale-10. The Parent Perceived Stress Scale-10 (PSS-10) is a validated 10-item self-assessment of caregiver stress on which respondents rate how regularly they felt a certain way in various situations during the last month.¹⁰ Questions are scored on a 5-point Likert scale (0 = never to 4 = always); items are summed into a total score, with higher scores indicating greater perceived stress.¹¹ This measure exhibited good internal consistency in our sample (Cronbach's $\alpha = 0.88$).

Penn State Worry Questionnaire. The Penn State Worry Questionnaire (PSWQ) is a 16-item scale designed to capture respondents' worry. Items are rated on a 5-point Likert scale (1 = not at all typical to 5 = very typical). Items are summed into a total worry score (<39 indicates low, 40-59 indicates moderate, 60-80 indicates high worry). Scores over 45 indicate generalized anxiety disorder (GAD). The PSWQ has been validated across cultures.¹² The scale exhibited excellent internal consistency in our sample (Cronbach's $\alpha = 0.92$).

Beck Anxiety Inventory. The Beck Anxiety Inventory is a 21-item self-report inventory that assesses common symptoms of anxiety over the last week (eg, numbness/tingling, fear of the worst happening). Items are scored on a 4-point Likert scale (0 = not at all to 3 = severely-it bothered me a lot) and then summed into a total anxiety score (≤ 21 indicates minimal/mild, 22-35 indicates moderate, and ≥ 36 indicates severe anxiety).^{13,14} The measure exhibited excellent internal consistency in this sample (Cronbach's $\alpha = 0.92$).

Food Allergy Self-Efficacy Scale for Parents. The Food Allergy Self-Efficacy Scale for Parents (FASE-P) measures parental confidence in their ability to manage their child's FA. Subdomains include managing social activities, precaution and prevention, allergic treatment, food allergen identification, and seeking information about FA. Each item is rated from 0 to 100 and a mean score is calculated. Higher scores indicate greater FA-related self-efficacy. The FASE-P offers excellent reliability over time in a general FA population.¹⁵ The measure exhibited excellent internal consistency in this sample (Cronbach's $\alpha = 0.91$).

Spence Preschool Scale, Spence Child Anxiety Scale, and Spence Child Anxiety Scale for Parents. The Spence Child Anxiety Scales (SCAS) are a set of assessments completed by children and parents regarding separation anxiety, physical injury fears, social phobia, obsessive compulsive, panic, agoraphobia, generalized anxiety, and overall anxiety. Specifically, the Spence Preschool Scale is a 28-item assessment completed by parents of children aged 3-6 years using a 5-point Likert scale (0 = not at all true to 4 = very often true).¹⁶ The SCAS and the SCAS for parents (SCAS-P) are both 38-item scales completed by children aged 7-15 years and their parents, respectively, using a 4-point Likert scale (0 = never to 3 = always).¹⁷ The SCAS is child self-reported answers, and the SCAS-P is a parent report about their child's anxiety symptoms. In this cohort, these scales exhibited high internal consistency (Cronbach's $\alpha \geq 0.87$ for all).^{18,19} Norm data regarding the preschool scale was based on a

TABLE I. Demographics of caregiver respondents

Characteristic (n = total respondents)	% (n)
Age (y), mean (SD) (n = 410)	34.9 (5.05)
Role (n = 409)	
Mother	95.8% (392)
Father	3.2% (13)
Other	1.0% (4)
Race/ethnicity (n = 404)	
African American	0.2% (1)
Asian	1.7% (7)
Hispanic	2.0% (8)
White	94.6% (382)
Other	1.5% (6)
Self-reported mental health conditions (n = 410)	
Anxiety	37.6% (154)
Depression	17.1% (70)
Educational level (n = 406)	
High school	4.4% (18)
Some college	12.3% (50)
College degree	42.6% (173)
Graduate degree or higher	40.6% (165)
Family income (n = 402)	
<\$100,000 annually	45.3% (182)
>\$100,000 annually	54.7% (220)
Marital status (n = 400)	
Single	4.8% (19)
Married	92.5% (370)
Divorced	2.3% (9)
Separated	0.5% (2)
Location survey completed (n = 410)	
Online	89.8% (368)
Conference	10.2% (42)
No. of children with FPIES (n = 410)	
1	91.0% (373)
2	8.3% (34)
3	0.7% (3)
Have FPIES emergency plan (n = 409)	71.1% (291)
Entire household avoids FPIES trigger (n = 409)	22.2% (91)

FPIES, Food protein-induced enterocolitis syndrome; SD, standard deviation.

cohort of 1368 Australian preschoolers,¹⁶ for the child scale was based on a sample of 2052 healthy Australian children aged 8-12,²⁰ and the parent scale was from 261 Australian and Dutch controls.¹⁹

Statistical analysis

Not all survey respondents completed every measure; thus sample size for the measures varied. If a caregiver did not entirely complete a measure, a total score was not calculated for that survey; however, if specific subscales were completed within a survey, subscale scores were calculated. Descriptive statistics were used for analysis. Continuous data were described as mean and standard deviation (SD). Our hypotheses were assessed using independent samples *t*-tests to compare mean survey scores. Pearson correlation was used to assess relationships among psychosocial domains. All statistical analyses were completed using SPSS statistical software, 24th edition (SPSS Inc., Chicago, IL). A *P* value <.05 was considered statistically significant.

TABLE II. Characteristics of children represented

Characteristic (n = total respondents)	% (n)
Age (y), mean (SD) [range] (n = 408)	3.0 (2.6) [2-19]
Female children (n = 274)	50.4% (138)
Atopic comorbidities (n = 409)	
Atopic dermatitis	34.0% (139)
IgE-mediated food allergy	24.4% (99)
Allergic rhinoconjunctivitis	17.4% (71)
Asthma	13.7% (56)
Parent-reported mental health conditions (n = 409)	
Anxiety	7.1% (29)
Depression	0.2% (1)
School/daycare attendance (n = 409)	
Attends	53.1% (217)
Does not attend	46.9% (192)
Does not attend due to FPIES	54.0% (102)
Food groups avoided due to FPIES (n = 441)	
Grains	60.5% (267)
Cow's milk	52.6% (232)
Vegetables	43.1% (190)
Fruits	38.3% (169)
Soy	37.2% (164)
Egg	23.4% (103)
Meats	18.1% (80)
Peanut	12.2% (54)
Poultry	12.0% (53)
Fish	9.3% (41)
Tree nut	8.4% (37)
Shellfish	5.9% (26)
Other (ie, oils, dyes, cocoa, sesame)	9.8% (43)
Evaluated in ED for acute FPIES reaction (n = 407)	57.5% (234)
Admitted for acute FPIES reaction (n = 408)	24.5% (100)

ED, Emergency department; FPIES, food protein–induced enterocolitis syndrome; SD, standard deviation.

RESULTS

Participant characteristics

The majority of the 410 respondents were mothers (95.8%, n = 392 of 409), white (94.6%, n = 382 of 404), and with a college degree or higher (83.2%, n = 338 of 406). Anxiety and depression were commonly self-reported in 37.6% (n = 154 of 404) and 17.1% (n = 70 of 404), respectively (Table I).

Demographic data for the 441 children represented are displayed in Table II. The mean age was 3.0 years (SD = 2.6). Atopic comorbidities were common, including atopic dermatitis (34.0%, n = 139 of 409) and IgE-mediated FA (24.4%, n = 99 of 409). Although the survey did not ask specifically about eosinophilic gastrointestinal disease, caregivers were asked to report any other medical conditions and 1 child was reported to have eosinophilic gastritis. The food groups most commonly avoided due to FPIES were grains, milk, and vegetables. More than half of the children attended daycare/school (53.1%, n = 217 of 409), but of those not attending (46.9%, n = 192 of 409), more than half were not attending due to FPIES (54.0%,

n = 102 of 192). Children not in daycare/school due to FPIES were young: the majority (98%, n = 100 of 102) of those not attending were under 5 years old.

Caregiver psychosocial functioning

Psychosocial assessment results are shown in Table III. On the FAQL-PB, caregivers (n = 295) reported a mean score of 3.4 (SD = 1.4; range = 0.06–6), corresponding to moderately to quite a bit limited/troubled. The highest levels of burden were noted in restaurant choice, vacation plans, and social engagement. Compared with the 2004 US validation cohort of caregivers of children with IgE-mediated FAs,⁹ the burden in FPIES caregivers was significantly higher (mean = 3.0 vs 3.4; $P < .001$). There were no statistical differences between the 2004 cohort and this cohort with regard to respondent caregiver role, race, income, or education level. However, the mean age of the children in the IgE-mediated cohort was 6.2 years, versus 3 years in the FPIES cohort.

On the PSS-10, caregivers (n = 237) reported a mean stress score of 20.6 (SD = 6.6; range = 3–35), corresponding to moderate stress. On the PSWQ, caregivers (n = 230) reported a mean score of 54.0 (SD = 12.1; range = 20–80), corresponding to moderate worry, and 77% (n = 176 of 230) of respondents had scores reflective of GAD.

To measure self-efficacy, the FASE-P was completed by 250 caregivers, with a mean score of 63.9 (SD = 17.12; range = 27–98) (Table IV). Compared with the 2015 UK-based validation cohort published by Knibb et al,¹⁵ self-efficacy surrounding FA management was significantly lower in caregivers of children with FPIES compared with caregivers of children with IgE-mediated FA (mean = 63.9 vs 76.1; $P < .001$). Similar to our cohort, their respondents were primarily female and recruited from an FA advocacy group's website and associated social media.¹⁵

Child anxiety

Results of the Spence assessments and published norms are displayed in Table V. Caregivers' ratings of their preschoolers' (n = 86) separation anxiety, obsessive-compulsive disorder (OCD), and general anxiety symptoms were significantly higher than published norms, (all $P < .05$). Children's (n = 11, aged 7–15) self-reported panic, OCD, general anxiety, and total anxiety symptoms were significantly lower than published norms (all $P < .05$). Conversely, caregivers' ratings of their children's (n = 14) separation anxiety, general anxiety, and total anxiety were significantly higher than published norms (all $P < .05$). FPIES caregivers and children strongly agreed on their perceptions of child anxiety on the SCAS and SCAS-P ($r = 0.92$, $P < .001$).

Associations among demographic variables, quality of life, anxiety, and self-efficacy

There was positive correlation among HRQoL, stress, worry, and anxiety scores, and these were negatively associated with FA self-efficacy scores (Figure 1). We hypothesized that lower income, greater number of food groups avoided, more than 1 child with FPIES, caregiver-reported anxiety/depression, and keeping a child out of daycare/school due to FPIES would be associated with poorer HRQoL, greater stress, worry, and anxiety, and lower FA-related self-efficacy. Income level $< \$100,000$ was associated with poorer HRQoL ($P = .039$) and lower FA-related self-efficacy ($P = .028$), but was not related to stress, worry, or anxiety. Caregivers whose child avoided a greater number of food

TABLE III. Food allergy-related quality of life, stress, worry, and anxiety in caregivers of children with FPIES

Assessment	Mean (SD)	Range of responses	Range of survey
Food Allergy Quality of Life-Parental Burden (n = 295)	3.4 (1.4)	(0.1-6)	(0-6)
Perceived Stress Scale-10 (n = 237)	20.6 (6.6)	(3-35)	(0-40)
Penn State Worry Questionnaire (n = 230)	54.0 (12.1)	(20-80)	(0-80)
Beck Anxiety Inventory (n = 216)	15.4 (11.0)	(0-51)	(0-63)

Higher scores indicate higher burden, stress, worry, and anxiety, respectively. The completion rates were 72.0% (n = 295 of 410) for Food Allergy Quality of Life-Parental Burden, 57.8% (n = 237 of 410) for Perceived Stress Scale-10, 56.1% (n = 230 of 410) for Penn State Worry Questionnaire, and 52.7% (n = 216 of 410) for Beck Anxiety Inventory.

FPIES, Food protein–induced enterocolitis syndrome; SD, standard deviation.

groups reported worse HRQoL ($r = 0.386$; $P < .001$), higher total anxiety among preschool-aged children ($r = 0.262$; $P = .013$) and elementary school-aged children ($r = 0.594$; $P = .025$), and poorer FA-related self-efficacy ($r = -0.282$; $P < .001$). The number of food groups avoided was unrelated to stress, worry, or anxiety in caregivers. After adjustment for other FPIES food triggers, caregivers who reported their child avoided cow's milk due to FPIES reported poorer HRQoL ($P < .001$), higher stress ($P = .001$), and lower FA-related self-efficacy ($P = .013$). Avoiding cow's milk was not associated with any of the other metrics assessed. Caregiver anxiety and/or depression or having more than 1 child with FPIES was not significantly associated with any psychosocial domains. Caregivers who reported that their child was not attending daycare/school due to FPIES had poorer HRQoL ($P < .001$), higher stress ($P = .014$), greater worry ($P = .004$), and higher total anxiety among preschool-aged children ($P = .032$), compared with caregivers whose children were out of school for other reasons.

DISCUSSION

The full psychosocial impact of FPIES on caregivers and affected children remains to be defined. Prior studies have identified that mothers of children with IgE-mediated FA have increased anxiety and stress compared with mothers of children without chronic illness, yet research has been lacking regarding the psychosocial impact of FPIES.^{21,22} To date, only 1 study has used surveys to evaluate the psychosocial impact of FPIES and demonstrated impaired HRQoL in caregivers.⁸ To our knowledge, no prior studies have evaluated the psychosocial impact of FPIES on affected children. Our study addresses these gaps in the literature and is one of the first to examine HRQoL, stress, worry, anxiety, and FA-related self-efficacy among a large cohort of caregivers and their children. Most caregivers in our sample reported moderate stress, and many reported significant worry. Indeed, three-quarters of the sample reported PSWQ scores suggestive of a possible diagnosis of GAD, which is notably higher than the 6.6% lifetime prevalence among the general population.²³ In our sample, caregivers reported significant burden associated with FPIES. When compared with burden in an IgE-mediated FA cohort,⁹ the burden in our sample of

TABLE IV. Food Allergy Self-Efficacy Scale-Parents in caregivers of children with FPIES

	n	Mean (SD)	Range of responses	Range of survey
Food Allergy Self-Efficacy-Parents Total	250	63.9 (17.1)	(27-98)	(0-100)
Managing social activities	260	52.2 (25.7)	(0-100)	(0-100)
Precaution and prevention	250	68.4 (19.3)	(18.3-100)	(0-100)
Treatment of food allergy	260	78.7 (20.3)	(13.7-100)	(0-100)
Food allergen identification	260	80.7 (17.3)	(13.7-100)	(0-100)
Seeking information	254	50.6 (22.8)	(0-100)	(0-100)

Higher FASE-P scores indicate higher self-efficacy. The scale was completed by 61.0% (n = 250 of 410) of respondents.

FASE-P, Food Allergy Self-Efficacy for Parents; FPIES, food protein–induced enterocolitis syndrome; SD, standard deviation.

caregivers was significantly higher. Although there may be a historical difference between the caregivers of children with FPIES and IgE-mediated FA samples (ie, the IgE-mediated paper was published in 2004),⁹ our findings align with previously published data, indicating that the burden of disease is different for caregivers of children with FPIES compared with caregivers of children with IgE-mediated FA.⁸ Further compounding the increased burden in this condition is the evidence that self-efficacy in caregivers of children with FPIES may be lower than that of IgE-mediated FA. Our findings warrant replication in other cohorts, particularly a general population sample who has not self-selected to attend an FPIES conference or participates in an online support group. Regardless, these findings are notable and indicate that many caregivers experience significant burden, stress, worry, and anxiety related to FPIES, along with low self-efficacy and would benefit from increased psychosocial support.²³

Our results also indicate that there may be certain demographic and medical characteristics that may help allergists identify caregivers especially at risk for poor psychosocial functioning related to FPIES, such as lower income (related to worse HRQoL and lower FA-related self-efficacy), avoiding cow's milk due to FPIES (related to worse HRQoL, more stress, and lower FA-related self-efficacy), and a greater number of foods avoided due to FPIES (related to worse HRQoL and greater child anxiety). Caregivers of lower financial means, whose children avoid cow's milk and/or whose children have to avoid a greater number of foods, may benefit from additional psychosocial support such as assistance from social work to address financial barriers to managing FPIES, meeting with a dietician to learn how to identify allergen alternatives and/or meal plan in the context of lower socioeconomic means, and psychotherapeutic consultation and treatment. Given the greater psychosocial distress related to lower income, it will be particularly important to repeat this study in a sample with broader socioeconomic representation.

Furthermore, allergists may want to bear in mind that reducing the number of foods a child avoids due to FPIES may improve HRQoL. Offering food challenges to either (1) confirm a questionable FPIES diagnosis or (2) assess whether a child may have developed tolerance to an FPIES allergen, and subsequently

TABLE V. Spence Assessment Scale scores in children with FPIES and their caregivers

Subscale	Preschool		Child		Parent	
	FPIES (n = 86)	Norm (n = 1368), Spence (2001) ¹⁶	FPIES (n = 11)	Norm (n = 2052), Yule (1997) ²⁰	FPIES n = 14)	Norm (n = 261), Nauta (2004) ¹⁹
Panic	—	—	2.7 (2.3)*	4.4 (4.9)	2.9 (3.4)	1.0 (1.6)
Separation anxiety	4.5 (4.6)*	3.2 (3.1)	4.5 (2.0)	4.9 (3.8)	5.5 (4.5)*	2.6 (2.8)
Physical injury	6.1 (5.2)	6.6 (4.6)	3.7 (2.6)	3.7 (3.0)	3.6 (2.4)	2.6 (2.3)
Social phobia	4.7 (4.9)	5.7 (4.7)	5.3 (3.5)	6.7 (4.1)	4.8 (4.4)	4.2 (2.8)
OCD	2.1 (3.0)*	1.4 (2.1)	1.3 (1.9)***	6.1 (4.0)	1.5 (1.7)	1.1 (1.7)
General anxiety	4.1 (4.9)*	2.9 (3.1)	3.9 (1.9)***	6.4 (3.8)	5.6 (3.7)*	2.7 (2.0)
Total anxiety	21.4 (18.6)	19.8 (13.7)	21.0 (10.3)**	32.1 (18.7)	23.9 (16.3)*	14.2 (9.7)

Means with standard deviations in parentheses are indicated.

Caregivers complete preschool and parent assessments; the child completes the child scale. Completion rates for the preschool, child, and parent scales were 79.6% (n = 86 of 108), 39.3% (n = 11 of 28), and 50.0% (n = 14 of 28), respectively. There was a strong correlation between child assessment total anxiety score and parent total anxiety score ($r = 0.92$; $P < .001$).

FPIES, Food protein–induced enterocolitis syndrome; OCD, obsessive-compulsive disorder.

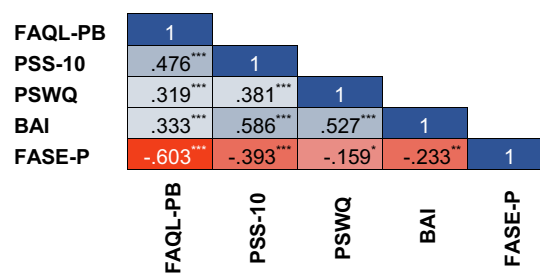
*** $P < .001$, ** $P < .01$, * $P < .05$ difference between scores in our FPIES cohort and norm cohorts.

“de-labeling” FPIES triggers, may serve to improve the mental health of caregivers and children. Based on our data, this may be especially true for caregivers whose children avoid milk. In a study of mothers of children with IgE-mediated FA, both children and mothers had improved HRQoL in the 3–6 months after a challenge and improvements in maternal and child mental health were irrespective of the challenge outcome.²⁴ The psychological impact of FPIES food challenges is not known and represents an area of further research.

All of our psychosocial domains correlated moderately, and all were negatively associated with FA-related self-efficacy. As such, improving self-efficacy for managing FPIES may improve caregiver HRQoL. Self-efficacy in the caregiver cohort was low, especially in the information-seeking subdomain. Allergists, nurses, and dietitians may play a role in improving the self-efficacy of caregivers through increasing understanding of food allergen identification, reaction prevention and management, and referring patients to appropriate high-quality venues to learn more information about the condition. Psychologists and social workers can provide invaluable guidance in navigating social interactions related to FPIES and assisting caregivers in managing stress and worry related to FA.

In this cohort, caregivers who reported that their child was out of school/daycare due to FPIES had poorer HRQoL, higher stress, worry, and anxiety compared with caregivers of children who were out of school for other reasons. In addition to arming caregivers with the information needed to keep their children safe at home, allergists have a responsibility to advocate for their patients' safety in daycares/schools and ensure that these facilities have the understanding necessary to identify and take the initial steps in the management of an acute FPIES reaction.

In our sample, parent and child anxiety scores correlated strongly. Although causation cannot be determined in this sample, anxiety behavior is frequently modeled by caregivers to children; thus, improving caregiver mental health has the potential to benefit the entire family. Interventions that improve the mental health of caregivers and children, through connection to a psychologist, may be helpful. In addition to access to nurse educators, psychologists, social workers, and dietitians, in person or virtual support from other families with FPIES may improve HRQoL and self-efficacy. A study that evaluated HRQoL and child anxiety after children with FA attended a week-long activity



*** $p < 0.001$, ** $p < 0.01$, * $p < 0.05$

FIGURE 1. Correlations between quality of life, stress, worry, anxiety, and self-efficacy in caregivers of children with FPIES. Higher FAQL-PB, PSS-10, PSWQ, and BAI scores indicate higher burden, stress, worry, and anxiety, respectively. Higher FASE-P scores indicate higher self-efficacy. Responses to each of these questionnaires correlated negatively with the FASE-P, which measures self-efficacy. BAI, Beck Anxiety Inventory; FAQL-PB, Food Allergy Quality of Life-Parental Burden; FASE-P, Food Allergy Self-Efficacy for Parents; FPIES, food protein–induced enterocolitis syndrome; PSS-10, Parent Perceived Stress Scale-10; PSWQ, Penn State Worry Questionnaire.

holiday with other children with FA found that children adopted more health-related behaviors, had a reduction in overall anxiety, and had improved HRQoL and confidence. Some benefits lasted as long as 6 months after the holiday.²⁵

Our study has many strengths and, given the lack of data regarding the psychosocial impact of FPIES, adds meaningfully to the literature. Results were based on large sample sizes, assessed multiple psychosocial domains, and the measures offered excellent validity. Our study has several limitations. Although this is the largest cohort of FPIES caregivers reported, the response rate comprised only 7.1% of I-FPIES at the time of the survey. Families who elected to complete the surveys may represent the most severe or complicated cases. This is a cross-sectional study, so no causal statements can be made. Our caregiver cohort primarily comprised white, married, well-educated mothers, which may limit generalizability. Furthermore, household income was stratified as less than or more than

\$100,000, which precludes a more granular analysis of income as a contributing factor to stress related to FPIES. Families self-identified as having a child with FPIES and reported their own comorbidities, foods avoided, and reaction histories. However, FPIES is diagnosed predominantly by caregiver-reported history and only confirmed by oral food challenge in cases when the history is unclear.⁶ Caregivers self-reported their history of anxiety or depression, and these diagnoses could not be confirmed with medical records. In future studies, a more rigorous assessment of underlying FPIES triggers as well as mental health diagnoses is essential. Norm data were from different cohorts and not reflective of child-parent dyads as in our study. This may impact our ability to directly compare FPIES caregiver and child scores from our study with norm data. Furthermore, we could not find normative data for each of the Spence assessments from a single cohort, and different “norm” cohorts were used for each discrete assessment, which complicates our ability to understand these results in relation to each other.

CONCLUSIONS

Caregivers experience a high degree of burden and psychosocial distress related to their child's FPIES diagnosis, which is related to lower self-efficacy. Demographic and medical variables related to poorer HRQoL include lower income, avoidance of multiple food triggers, and avoidance of cow's milk due to FPIES. Interventions that address parent and child anxiety and parental self-efficacy are sensitive to financial barriers, and the number and type of foods avoided are likely to have the greatest impact on families. Findings from our study may help providers identify patients and families with FPIES who are at risk for higher psychosocial burden and who may benefit from psychological support.

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ONLINE REPOSITORY

DEMOGRAPHICS AND BACKGROUND QUESTIONNAIRE

****If you have 2 parents/guardians present or multiple children with FPIES who would like to fill out surveys, please ask and we will provide additional copies of the surveys.****

QUESTIONS FOR PARENT/GUARDIAN OF CHILD WITH FPIES

1. What is **your** relationship to the person with FPIES?
 - a. Mother
 - b. Father
 - c. Other—please specify _____
2. What is **your** gender?
 - a. Male
 - b. Female
3. How old are **you**?
 - a. Please specify _____
4. What is **your** marital status?
 - a. Single
 - b. Married
 - c. Separated
 - d. Divorced
 - e. Widowed
5. What is **your** race?
 - a. African American
 - b. Asian
 - c. Hispanic
 - d. White
 - e. Native American
 - f. Native Hawaiian, Pacific Islander
 - g. Multi-Race, Non-Hispanic
 - h. Other—please specify _____
6. What is your annual household income?
 - a. <\$100,000/year
 - b. >\$100,000/year
7. What is **your** highest education level?
 - a. High school
 - b. Some college
 - c. College
 - d. Graduate degree
 - e. Other—please specify _____

FIGURE E1. Survey for caregivers of children with FPIES. Demographics and background questionnaire provided to caregivers of children with FPIES. The survey asked about basic demographic data for the caregivers and their affected child/children, foods avoided due to FPIES, FPIES reaction history, and comorbid conditions of the child and caregiver. *FPIES*, Food protein–induced enterocolitis syndrome.

8. How many children do you have?
a. Please specify _____
9. How many of your children have FPIES?
a. Please specify _____
10. What are the age(s) of your child(ren) with FPIES?
a. Please specify _____
11. Does your child/children with FPIES attend school or daycare?
a. Yes
b. No
If **no**, are you keeping them out due to concern over their FPIES?
a. Yes
b. No
12. Does your child/children with FPIES have a written FPIES Emergency Plan?
a. Yes
b. No
13. Does everyone in your household follow the same avoidance diet as your child/children with FPIES?
a. Yes
b. No
14. Which food(s) does **your child/children** need to avoid due to FPIES? Please check and specify (where indicated) all that apply for each child with FPIES.

	Child #1	Child #2	Child #3	Child #4
a. Milk				
b. Soy				
c. Egg				
d. Peanuts				
e. Tree nuts (specify which ones)				
f. Fish (specify which ones)				
g. Shellfish (specify which ones)				
h. Grains (specify which ones)				
i. Meats (specify which ones)				
j. Poultry (specify which ones)				
k. Fruits (specify which ones)				
l. Vegetables (specify				

FIGURE E1. (CONTINUED).

which ones)				
m. Other (specify which ones)				

15. Has your child/children ever been to the Emergency Room for an FPIES reaction?
- No
 - Yes
16. Has your child/children ever been admitted to the hospital overnight for an FPIES reaction?
- No
 - Yes
17. What were the symptoms of your child's **worst** FPIES reaction (circle all that apply)? If multiple children with FPIES, indicate worst reaction for any child.
- Vomiting, 1-3 episodes within 1-4 hours after eating culprit food
 - Vomiting, ≥ 4 episodes within 1-4 hours after eating culprit food
 - Decreased activity level
 - Lethargy
 - Pale-appearing skin
 - Unable to tolerate liquids by mouth
 - Diarrhea, non-bloody, within 24 hours of eating culprit food
 - Diarrhea, bloody, within 24 hours of eating culprit food
 - Hypotension (low blood pressure)
 - Hypothermia (low body temperature)
 - Other (please specify) _____
18. What interventions were required to treat your child's **worst** FPIES reaction (circle all that apply)? If multiple children with FPIES, indicate worst reaction for any child.
- Home management
 - Emergency Room visit
 - Overnight hospital admission
 - Intravenous (IV) fluids
 - Oral steroids
 - Intravenous (IV) steroids
 - Ondansetron (a.k.a. zofran)
 - Other (please specify) _____
19. Does **your child/children with FPIES** have IgE-mediated food allergies in addition to FPIES?
- No
 - Yes
- If **yes**, which food(s)? _____
20. Does **your child/children with FPIES** have any other medical conditions?
- Celiac disease
 - Asthma
 - Atopic dermatitis (a.k.a. eczema)
 - Allergic rhinoconjunctivitis (a.k.a. hayfever, seasonal allergies)

FIGURE E1. (CONTINUED).

- e. Anxiety
- f. Depression
- g. Other (please specify) _____

21. Do **you** have any medical conditions?
- a. FPIES
 - b. IgE-mediated food allergies
 - c. Celiac disease
 - d. Asthma
 - e. Atopic dermatitis (a.k.a. eczema)
 - f. Allergic rhinoconjunctivitis (a.k.a. hayfever, seasonal allergies)
 - g. Anxiety
 - h. Depression
 - i. Other (please specify) _____

QUESTIONS FOR CHILD (AGE ≤ 18 YEARS OLD) WITH FPIES

May complete with parental assistance

1. What is your gender?
 - a. Male
 - b. Female
2. How old are you?
 - a. Please specify _____
3. What is your race?
 - a. African American
 - b. Asian
 - c. Hispanic
 - d. White
 - e. Native American
 - f. Native Hawaiian, Pacific Islander
 - g. Multi-Race, Non-Hispanic
 - h. Other—please specify _____
4. What is your parents' highest education level?
 - a. High school
 - b. Some college
 - c. College
 - d. Graduate degree
 - e. Other—please specify _____

FIGURE E1. (CONTINUED).

Only complete questions below if the parent/guardian indicated they have MORE THAN ONE CHILD WITH FPIES (#9 in the parent questionnaire). (These are the same as #14-20 in the parent questionnaire).

5. Which food(s) do you need to avoid due to FPIES?
 - a. Milk
 - b. Soy
 - c. Egg
 - d. Peanuts
 - e. Tree nuts (specify which ones)
 - f. Fish (specify which ones)
 - g. Shellfish (specify which ones)
 - h. Grains (specify which ones)
 - i. Meats (specify which ones)
 - j. Poultry (specify which ones)
 - k. Fruits (specify which ones)
 - l. Vegetables (specify which ones)
 - m. Other (specify which ones) _____
6. Have you ever been to the Emergency Room for an FPIES reaction?
 - a. No
 - b. Yes
7. Have you ever been admitted to the hospital overnight for an FPIES reaction?
 - a. No
 - b. Yes
8. What were the symptoms of your worst FPIES reaction (circle all that apply)?
 - a. Vomiting, 1-3 episodes within 1-4 hours after eating culprit food
 - b. Vomiting, ≥ 4 episodes within 1-4 hours after eating culprit food
 - c. Decreased activity level
 - d. Lethargy
 - e. Pale-appearing skin
 - f. Unable to tolerate liquids by mouth
 - g. Diarrhea, non-bloody, within 24 hours of eating culprit food
 - h. Diarrhea, bloody, within 24 hours of eating culprit food
 - i. Hypotension (low blood pressure)
 - j. Hypothermia (low body temperature)
 - k. Other (please specify) _____

FIGURE E1. (CONTINUED).

9. What interventions were required to treat your worst FPIES reaction (circle all that apply)?
 - a. Home management
 - b. Emergency Room visit
 - c. Overnight hospital admission
 - d. Intravenous (IV) fluids
 - e. Oral steroids
 - f. Intravenous (IV) steroids
 - g. Ondansetron (a.k.a. zofran)
 - h. Other (please specify) _____
10. Do you have IgE-mediated food allergies in addition to FPIES?
 - a. No
 - b. Yes

If **yes**, which food(s)? _____
11. Do you have any other medical conditions?
 - a. Asthma
 - b. Atopic dermatitis (a.k.a. eczema)
 - c. Allergic rhinoconjunctivitis (a.k.a. hayfever, seasonal allergies)
 - d. Anxiety
 - e. Depression
 - f. Other (please specify) _____

FIGURE E1. (CONTINUED).