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Quality of life associated with maternal anxiety disorder in Russian children and adolescents with food allergy

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Abstract

Background: Food allergy negatively impacts the quality of life (QoL) and has been associated with increased maternal anxiety. There is currently a lack of data assessing QoL of food allergic children and adolescents in Russia. We aimed to evaluate the performance of the Food Allergy Quality of Life Questionnaires (FAQLQ) measures in a Russian sample of children, adolescents and mothers and to investigate association between child QoL and maternal general anxiety.

Methods: FAQLQ and Food Allergy Independent measures (FAIM) were translated to Russian to be completed by participants. Mothers also filled the General Anxiety Disorder (GAD-7) questionnaire. Reliability, construct and discriminant validity of the FAQLQs and association between FAQLQ scores and general anxiety were assessed.

Results: 142 participants completed FAQLQ and FAIM. 126 mothers completed GAD-7 questionnaire. All FAQLQs showed excellent internal consistency ($\alpha > 0.94$). The means for the FAQLQ-PF; -CF and -TF varied according to the number of foods avoided and symptoms severity, FAIM and GAD scores ($\eta p2$ 0.40 $p < 0.001$). 1 in 5 mothers had GAD-7 score indicative of moderate to severe anxiety. Association strength between GAD and FAQLQ increased with age. GAD score was associated with FAQLQ-PF score, controlling for multiple confounders.

Conclusion: The FAQLQ showed good reliability and validity in Russian. This study identified number of foods avoided and reported reaction severity being associated with greater QoL impairment in Russian children and adolescents affected by food allergy. The significant association found between general anxiety in parents and QoL in children and adolescents has practice, screening and resource implications.

Introduction

Food allergy is a major public health concern affecting up to 20 million European citizens, including around 1 in 20 infants, with high costs to public health services [1-4]. Ninety percent of food allergy is caused by 8 foods (milk, egg, wheat, soy, peanut, tree nuts, fish, and shellfish). Allergy to peanut, tree nut, fish, shellfish, and sesame seed are considered to be life-long in 80-90% of cases, and potentially severe. Reactions can occur upon initial exposure, and even from minimal quantities. Symptoms range from mild (itching, swelling, hives, etc.) to systemic reactions (gastrointestinal, cardiac, respiratory, or multi-system). Allergen avoidance and self-injectable epinephrine is the current standard of treatment for food allergy, but accidental ingestion is common, causing frequent and sometimes life-threatening reactions [5-9]. Admission rates for anaphylaxis have increased approximately 3-fold between 2005 and 2012 [5,6,10-12]. In the US, prevalence has doubled in 10 years, leading to >300,000 annual hospital visits with estimated costs of $24.8 billion annually [12].

Patient related outcome measures can be used in the evaluation and monitoring of health care interventions, in the assessment of best practice from the patients' perspective, and in screening for potential psychological problems. The results generated from research can have an impact on the provision of resources and on health and regulatory policy [13,14]. The Food Allergy Quality of Life Questionnaires (FAQLQ) are disease-specific developmentally appropriate measures [15-21] that have been developed to assess health related quality of life (HRQL) in food allergy for all age groups and parents and are the most frequently used HRQL tools in food allergy research and practice. These include the Parent Proxy Form (PF), the Child-form (CF), the Teen form (TF) and the Adult form (AF). The questionnaires can be used to measure cross-sectional differences in quality of life between patients at a point in time - or longitudinal changes in HRQL. Research has shown that FAQLQ measures are valid, reliable and are responsive to important clinical changes [22-24].

The development of food allergy specific outcome measures has allowed for an improved evidence-based understanding of the impact of food allergy (from the perspective of patients) for clinicians, researchers and policy makers. Significant provider-level heterogeneity in food allergy diagnosis/management and variations in advising/counselling patients regarding individual risk

and natural history of disease, together with diverse and unclear food labelling, has been shown to give rise to anxiety, uncertainty, confusion, worry, and low confidence in managing food allergy [15-21,24,25]. Thus, the main concerns relate principally to the psychological impact of living with food allergy, followed by the impact of dietary and social restrictions. The most significant impairment is anxiety and the persistent fear of an adverse reaction, which has more profound effects on emotional and social aspects of a patient's everyday life, than clinical reactivity induced by food intake [26]. Differences in impact depending on age have also been documented [25].

Eiser and Morse [27] outlined recommendations on the development and use of measures to assess HRQL in children with chronic diseases, including the importance of ensuring that the questionnaire is suitable in the context in which it is being utilised to ensure the validity, reliability and interpretation of the results. To the best of our knowledge, this is the first time that HRQL in children with food allergy has been measured in Russia using given instruments. Furthermore, at present there are no auto-injectors registered in Russia and general knowledge of food-induced anaphylaxis diagnosis and management is poor [28], which may in turn result in higher levels of anxiety for parents and patients.

In the present study, we examined (a) the performance of the FAQLQ measures in a Russian sample of parents, children and adolescents; and (b) the association between FAQLQ and general anxiety in mothers. We hope that our findings will contribute to ongoing work to develop an online manual of normed scores and to provide further evidence of the correlates of HRQL.

Methods

Design

In this prospective cross-sectional quantitative study, the sample consisted of children between the ages of 0 and 18 years with clinician diagnosed food allergy and their parents.

Measures

The Food Allergy Quality of Life Questionnaire is available in different versions, depending on the target individual: PF, CF and TF which assess the HRQL of patients with food allergy. It has

been found to have excellent reliability ($\alpha > 0.9$), and construct, cross-cultural, content and longitudinal validity [15-24].

The Food Allergy Independent Measure – Parent Form (FAIM) was developed to evaluate whether the FAQLQ measures those aspects of HRQL affected by food allergy specifically rather than the more general quality of life domains; it is therefore both independent and disease specific [15,16]. The FAIM has been shown to have good test-retest reliability with intraclass correlation coefficients between 0.76 and 0.87 and Lin's concordance correlation coefficients above 0.7 [17].

The Generalised Anxiety Disorder Questionnaire - 7 (GAD-7) is a self-administered questionnaire that is used as a screening tool and severity measure for generalised anxiety disorder, panic disorder, social anxiety, and Post Traumatic Stress Disorder (PTSD) [29]. The GAD-7 has a sensitivity of 89% and a specificity of 82% for GAD. The GAD-7 was completed by the parent.

Translation of the Measures

All measures were translated in Russian and back-translated according to WHO guidelines [30].

Procedure

The data were collected in the allergy department of the Veltischev Research and Clinical Institute for Paediatrics of the Pirogov Russian National Research Medical University, Moscow, Russia. The criteria for participation were that participants were clinically diagnosed with a food allergy, between the ages of 0 and 18 years and that the parent-proxy respondents were 18 years of age or over. Participants were recruited among patients considered 'food allergic' on the basis of a combination of parent- and/or self-reported clinical history and skin prick test/specific IgE. No oral food challenge has been performed.

Ethics

Prior to the study, protocol and research materials were reviewed and approved by the Ethics committee of the Veltischev Research and Clinical Institute for Paediatrics of the Pirogov Russian National Research Medical University.

Data analysis

Statistical analyses were performed using SPSS software (version 21.0; SPSS Inc., Chicago, IL, USA). Cronbach's alpha was used to test reliability of the FAQLQ questionnaires. Construct validity was examined with the Pearson's product-moment correlation coefficient. We expected a significant moderate correlation between the FAQLQ total scores and the FAIM total score.

Discriminant validity was evaluated through examination of means and standard deviations and by conducting a one-way analysis of co-variance (ANCOVA), controlling for age of food allergic participant in order to examine the distribution of FAQLQ scores (dependent variable). We expected FAQLQ responses to vary based on the following independent variables; number of symptoms (1-4+); number of allergies (1-4+); number of foods avoided (1-5+), most severe symptom experienced (skin, gastrointestinal, respiratory). Partial eta-squared (ηp2) or effect sizes (that express the amount of variance accounted for by one or more independent variables) were also calculated. Effect size emphasises the size of the difference rather than confounding with sample size. Cohen [31] provides partial eta squared values of .0099, .0588, and .1379 as benchmarks for small, medium, and large effect sizes, respectively.

The strength and significance of the hypothesised association between outcome variables FAQLQ (PF and TF separately) and GAD-7 score was examined using a multiple hierarchical linear regression. The regression controlled for child age; child sex, number of allergies, number of symptoms, and severity of symptoms. FAQLQ was entered in the last step.

Results

In total, 142 FAQLQ questionnaires were completed. These included 50 proxy-reports by parents of children aged 0 to 7 years, 44 children aged 8 to 12 years and 48 aged 13 to 18 years. In addition to FAQLQ questionnaires FAIM information was obtained in 142 participants. The mean age for children/adolescents in the sample was 9.9 years (SD, 4.8), 68% were male. Most of parents who completed the measures were mothers 87 (94%) and only these data were included into statistical analysis.

Table 1 shows the sample characteristics for experience of anaphylaxis, time since anaphylaxis, number of allergies and type of allergies. The mean number of allergies reported was 4.1 (+/-

3.3), with 70% reporting more than one allergy and 66% experiencing anaphylaxis within the last 12 months. There was a variety of foods involved with egg and peanut being the most prevalent.

Table 1. Sample characteristics: anaphylaxis, recency of anaphylaxis, atopic co-morbidity, number and type of allergies.

Characteristics	Mean (SD)
Number of allergies	4.1 (3.3)
Number of co-morbidities (atopic)	1.6 (0.8)
Number of symptoms	7.6 (5.0)
	Number (% of total reporting)
Anaphylaxis (yes)	99 (76.0)
Time since anaphylaxis	
(for those reported as having experienced this?)	
<6 months	17 (31.0)
6- 12 months	19 (35.0)
1 to 2 years	10 (19.0)
2 years +	8 (15.0)
Type of food causing allergic symptoms	
Peanut	49 (35.0)
Milk	44 (31.1)
Egg	57 (40.4)
Hazelnut	47 (33.3)
Almond	36 (26.0)
Walnut	45 (32.2)
Sesame	21 (15.0)
Fish	38 (27.1)
Shellfish	24 (17.0)
Fruit	62 (44.3)
Other	49 (42.0)

Food Allergy Quality of Life (FAQLQ) and Food Allergy Independent Measure (FAIM)

There was good agreement between FAQLQ-PF and FAQLQ-CF (r=0.62) and FAQLQ-TF (r=0.63). The internal consistency (i.e. reliability) of all measures was excellent (α >0.9).

Table 2. Food allergy-related quality of life, presented as a mean Food Allergy Quality of Life Questionnaires, Cronbach's Alpha (α) and Food Allergy Independent Measure scores for Parent Proxy and Child/Teen Self-Report.

Measure	Responder	Mean (SD)	Reliability (α)	Measure	Mean (SD)
FAQLQ-PF	Proxy-report			FAIM-PF	
0-6 years		3.50 (1.2)	0.92	0-6 years	3.7 (0.6)
7-12 years		3.63 (1.3)	0.95	7-12 years	3.7 (0.7)
FAQLQ-CF	Self-report			FAIM-CF	
7-12 years		3.9 (1.1)	0.94	7-12 years	3.8 (0.8)
FAQLQ-TF	Self-report			FAIM-TF	
13 years +		3.8 (1.7)	0.93	13 years +	3.6 (0.9)

FAQLQ, Food Allergy Quality of Life Questionnaires; FAIM, Food Allergy Independent Measure; CF, Child form; TF, Teen form; PF, Parent form.

There was a significant positive moderate correlation between the total scores for FAQLQ and FAIM, indicating good criterion validity (Table 3).

Table 3. Pearson Correlations (r) between Food Allergy Quality of Life Questionnaires and Food Allergy Independent Measures.

Measure	FAIM	p-value
FAQLQ-PF		
0-6 years	0.53	**0.0001**
7-12 years	0.62	**0.0001**
FAQLQ-CF		
7-12 years	0.60	**0.0001**
FAQLQ-TF		
13 years +	0.61	**0.0001**

FAQLQ, Food Allergy Quality of Life Questionnaires; FAIM, The Food Allergy Independent Measure; CF, Child form; TF, Teen form; PF, Parent form. Statistically significant results presented in bold.

The means and standard deviations for the FAQLQ-PF; -CF and -TF varied according to the number of allergies, the number of symptoms, the most severe symptom experienced, and the number of foods avoided, as reported by the respondent or parent (Table 4). The mean scores increased (HRQL decreased) on average at least one point on the scale, according to the number of reported food allergies, the number of reported symptoms and the number of foods avoided. HRQL also decreased for those whose most severe symptom was gastrointestinal and respiratory, compared to skin only symptoms.

Table 4. Total scores for different forms of Food Allergy Quality of Life Questionnaires; Discriminant Validity

Measure	FAQLQ-PF	FAQLQ-CF	FAQLQ-TF
	Mean (SD)	Mean (SD)	Mean (SD)
Number of reported food allergies			
1	2.8 (1.1)	3.1 (0.9)	3.1 (1.3)
2	3.7 (1.1)	4.6 (1.0)	3.9 (1.4)
3+	4.3 (1.3)	4.1 (0.9)	4.1 (1.4)
Number of reported Symptoms			
1	2.6 (0.8)	3.7 (1.1)	2.9 (1.2)
2	3.4 (1.2)	4.0 (1.5)	3.5 (1.5)
3 +	3.8 (1.2)	3.9 (1.1)	3.9 (1.3)
Number of Foods Avoided			
1	2.5 (1.1)	3.1 (1.4)	3.1 (1.6)
2	2.8 (1.1)	3.4 (1.0)	3.4 (1.2)
3	3.4 (0.9)	3.9 (1.1)	4.0 (1.3)
4+	4.2 (1.1)	4.3 (1.1)	4.4 (1.0)
Most Severe Symptoms			
(of those who reported severe symptoms)			
Skin	3.1 (1.2)	3.8 (1.2)	3.5 (1.4)
Gastrointestinal	3.7 (1.2)	-	3.6 (1.4)
Respiratory	3.8 (1.2)	4.0 (1.1)	3.8 (1.3)

FAQLQ, Food Allergy Quality of Life Questionnaires; CF, Child form; TF, Teen form; PF, Parent form.

To investigate if these differences were significant, we conducted an analysis of covariance (ANCOVA) with the FAQLQ-PF as the dependent variable (Table 5). The independent variables included the number of allergies, the number of symptoms, the most severe symptom experienced, and the number of foods avoided. FAQLQ PF significantly discriminated between the independent variables with large effect sizes (Partial eta-squared, ηp2). Although the pattern of scores suggest a strong trend, we did not have sufficient power to determine if differences were significant for the FAQLQ-CF or TF.

Table 5. Assessment of FAQLQ-PF Discriminant Validity, using analysis of variance (ANOVA)

	F	p-value	Partial Eta (ηp2) Squared
FAQLQ-PF			
Number allergies	2.39	**0.013**	0.42*
Number of symptoms	2.95	**0.001**	0.46*
Number of foods avoided	12.44	**< 0.001**	0.36*
Most severe symptom	3.74	**0.03**	0.10*

*Partial eta squared effect sizes small effect = 0.0099; medium effect = 0.0588; large effect = 0.1379 Statistically significant results presented in bold. FAQLQ-PF, Food Allergy Quality of Life Questionnaire - parent form.

Associations between General Anxiety Disorder and Food Allergy Quality of Life

In total, 126 GAD-7 questionnaires were completed. The mean score for GAD-7 was 5.3 (SD 4.0). This mean is significantly higher compared to norms for the general population [29] of 2.9 [t (df 1.28) = 6.704, p = 0.0001]. The GAD-7 mean was highest for parents of children aged 0 to 7 years (M 6.3, SD 3.5), followed by parents of children aged 8 to 12 years (M 5.0, SD 4.1), and parents of adolescents (M 4.6, SD 4.3). Furthermore, GAD-7 scores were higher for those with 3 or more allergies (M 6.6, SD 3.3) vs those with one allergy (M 4.5, SD 4.4) and higher for those who reported anaphylaxis (M 5.8, SD 4.1) than for those who did not (M 4.8, SD 3.8). More than 17% of the sample were above the threshold score (10 +) for possible clinical anxiety disorder and 29% were above the threshold score (8+) for panic, social anxiety and PTS disorders.

To test for the hypothesised association between FAQLQ and GAD-7 score, we carried out a series of hierarchical multiple linear regressions, using only those predictors found to be significant in previous analyses. The models controlled for child age; child sex, number of allergies, number of symptoms, and severity of symptoms (Table 6). Only FAQLQ and age of child remained a significant predictor for GAD-7, suggesting that FAQLQ has the strongest unique association with GAD-7 score, followed by child's age, keeping the other variables in the model constant (Table 6).

Table 6. Associations between Generalized Anxiety Disorder 7-item scale and Food Allergy Quality of Life Questionnaires: Linear Regression Model.

	Standardised Co-efficients Beta	t value	P value	95% CI Lower/Upper
FAQLQ-PF	0.59	3.6	**0.001**	0.81/2.80
Child age	-0.37	-2.4	**0.019**	-0.70/-0.06
Child sex	-0.23	-1.8	0.083	-4.02/0.25
Number allergies	-0.29	-1.7	0.082	-3.08/0.19
Number of symptoms	0.16	0.96	0.339	-1.04/2.96
Most severe symptom	-0.19	-1.1	0.284	-2.19/0.65
FAQLQ -TF	0.33	2.8	**0.007**	0.27/1.69
Child age	0.12	1.1	0.286	-0.16/0.54
Child sex	0.05	0.47	0.642	-1.6/2.67
Number allergies	0.12	0.97	0.334	-0.72/2.10
Number of symptoms	0.18	1.1	0.266	-0.93/3.31
Most severe symptom	0.04	.22	0.825	-1.29/1.62

FAQLQ, Food Allergy Quality of Life Questionnaires; TF, Teen form; PF, Parent form; Generalized Anxiety Disorder 7-item scale, GAD-7. Statistically significant results presented in bold.

Discussion

We examined the performance of the FAQLQ-PF; -CF and -TF measures in a Russian sample of children, adolescents and parents and investigated any associations with generalised anxiety disorder in mothers.

The FAQLQ scores reflect typical European means (average mean 3.2) for parent proxy report, for CF (average mean score 3.9) and TF forms (average mean score 3.9). All FAQLQ measures showed strong internal consistency, reliability, and criterion and discriminant validity. The means and standard deviations for the FAQLQ-PF; -CF and -TF varied according to the number of allergies, the number of symptoms, the most severe symptom experienced, and the number of foods avoided increasing (HRQL decreasing) on average at least one point on the scale. HRQL also decreased for those whose most severe symptom was gastrointestinal and respiratory, compared to skin only symptoms.

The mean score for GAD-7 was significantly higher compared to reported norms for the general population and was even higher for mothers of children aged less than 7 years. Greater than 17% of the sample were above the threshold score (10 +) for possible clinical anxiety disorder compared to 5% in general population norms and 29% were above the threshold score (8+) for panic, social anxiety and PTS disorders.

Maternal mental status may influence offspring health, with research showing maternal depression and anxiety being linked with significant changes in child HRQL scores [32,33] and even the levels of immunological biomarkers [34]. There is also some evidence of associations between maternal anxiety and depression and allergic symptoms in children [35], however, there is an apparent lack of studies investigating impact of maternal mental health on allergic children HRQL.

While any chronic condition can potentially affect developmental processes, the reverse is true - that is, a combination of physiological, environmental, and psychosocial factors can have an impact on the disease. Anxiety is thought to be problematic when its intensity and duration begin to impact one's functioning and quality of life. Food-allergic adolescents (12-25 years) have higher internalising problems such as anxiety, depression, relational difficulties, lower HRQL, and higher impact of psychological problems on everyday life, than healthy peers [18,24,25].

Research has shown that environmental factors, as opposed to genetics, play a more important role in the transmission of anxiety from parents to their adolescent children [36]. There was good

agreement between FAQLQ-PF and FAQLQ-CF with the mean scores for FAQLQ-CF only slightly higher than PF. Furthermore, the strongest predictors of anxiety as measured by the GAD-7 were parent and adolescents scores on the FAQLQ. Although these results provide only tentative evidence for the transmission of anxiety from parent to child, they do provide a good foundation for future research. Anxiety disorders can have serious consequences in children/adolescents and therefore proper identification and treatment of anxiety disorders is necessary and may improve not only psychological but also physical symptoms [37]. Because at present there are no auto-injectors registered in Russia and general knowledge of food-induced anaphylaxis diagnosis and management is poor [28], it presents an excellent basis on which to measure any consequent improvements due to treatment or intervention.

A limitation of this study is that food allergy diagnosis was defined as a combination of clinical history and skin prick test/specific IgE combination with no oral food challenge performed. Oral food challenges are not routinely performed in Russia which did not allow for food allergy 'gold standard' evaluation. However, this is unlikely to have influenced the outcomes of our study. While the GAD-7 was associated with FAQLQ-PF, it was also associated with FAQLQ-TF scores. Parental perception of teen FAQL has not been fully assessed. We are aiming to clarify it in the future research by using the FAQLQ-PFT. A lack of power for some of the age groups was a further limitation. We intend to carry out a larger study in the near future to further confirm these findings.

Despite these noted limitations, to our knowledge this is the first time that HRQL in children and adolescents with food allergy has been measured in Russia. The FAQLQ performed very well in terms of reliability and validity. Our results will add to ongoing work in the development of food allergy normed age scores to allow for precise measurement, interpretation of scores, and comparison across countries and cultures, in clinical and research settings. This will ensure greater precision in measurement in future studies in Europe and the US and throughout the world.

In addition, our findings on significant associations between generalised anxiety with HRQL will prove useful in further research on screening for potential psychological problems in food allergy, with implications for the provision of resources and on health and regulatory policy.

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