

Vitulia questionnaire: a new instrument to evaluate quality of life in children aged 4-7 years with food allergy

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ABSTRACT

Background: Food allergy (FA) negatively affects health-related quality of life (HR-QoL) of children and caregivers. To date, no questionnaire self-compiling assessing the HR-QoL in pre-school children with FA is available. The aim of this study is to develop and validate a self-administered, rapid and easy questionnaire to evaluate the HR-QoL in children ≥ 7 years with IgE-mediated FA. **Methods:** A two-center prospective study was conducted including children aged 4-7 years with IgE-mediated FA. The Vitulia questionnaire was administered to study participants at the baseline (T0) and after one month (T1). To assess the feasibility and reliability, the Vitulia questionnaire was compared with other two pre-existing questionnaires: FAQLQ-PF and the KiddyKindl, which were also tested at both T0 and T1. The validation phase aimed to assess the following psychometric properties: convergent validity, internal consistency, discriminant validity and sensitivity to change. **Results:** One hundred patients (62% male, mean age 5.4 ± 1.2 years) were enrolled. The Vitulia questionnaire showed a good internal consistency along with an excellent reliability and repeatability of the measure. Another noteworthy feature of the

questionnaire was its discriminant validity as demonstrated by the ability to provide different scores in subgroups, which have differences in terms of quality of life. On the other hand, the questionnaire seems not be sensitive to changes in health status over time. **Conclusions:** The Vitulia questionnaire represents a valid tool, quick and easy to interpret, which can be used to assess the quality of life in preschool children with IgE-mediated FA.

KEY WORDS

Food allergy, health-related quality of life, questionnaire, children

IMPACT STATEMENT

The assessment of health-related quality of life in children with food allergy represents an important aspect in the management of this disease in every age group. Therefore, a new self-administered questionnaire among children aged 4-7 years could be a further useful tool to evaluate health-related quality of life.

INTRODUCTION

Food allergy (FA) represents an emerging public health issue, with an increasing incidence in the last years [1]. FA is the most important cause of life-threatening hypersensitivity reactions and negatively affects the health-related quality of life (HR-QoL) of patients and their caregivers, determining anxiety, fear of accidental exposures and social isolation [2].

The evaluation of HR-QoL in patients with FA is paramount for obtaining the best clinical control in the management of this disease [2]. The assessment is performed through the administration of a standardized questionnaire, the Food Allergy Quality of Life Questionnaire (FAQLQ), submitted directly to patients aged ≥ 8 years or their parents if patients are younger than 8 years (FAQLQ-parent form). In the latter case, different versions are available according to the age of children [3,4,5,6]. The most recent Food Allergy Quality of Life Questionnaire-parent form10 (FAQLQ-PF10) was also found to be a validate tool, with an excellent reliability in patients with FA [7].

However, in order to better evaluate the burden of FA, it would be important to receive a feedback directly from the child, even in the preschool age.

To the best of our knowledge, no questionnaire self-compiling assessing the HR-QoL in pre-school children with FA is available thus far. The aim of the study was to develop and validate a self-administered, rapid and easy questionnaire to evaluate the HR-QoL in children younger than 7 years affected by IgE-mediated FA.

MATERIALS AND METHODS

A multicenter prospective study was conducted between March 2019 and March 2022. The study population included children aged 4-7 years with IgE-mediated FA from at least one year and followed at the Pediatric Allergology Unit, University Hospital “G. Martino” of Messina or at the Institute of Translational Pharmacology, National Research Council of Italy of Palermo. Non-IgE mediated FA and poor compliance were considered as exclusion criteria. The study was approved by the Ethics committee of the University of Messina (n° 27/19). Parents of each patient provided their informed consent. Anamnestic and clinical data were collected. Skin prick test, prick by prick test and specific IgE dosage were performed. The diagnosis of IgE-mediated FA was confirmed through an oral food challenge. The Vitulia questionnaire was developed by two Pediatric allergy Centers, the University Hospital “G. Martino” of Messina and National Research Council of Italy of Palermo. The name comes from the imagination of the creator of the project (GBP). The Vitulia questionnaire was established based on current best practice for developing and validating scales for health, social, and behavioral research [8]. This instrument was first tested on a small sample of the target population to assess its feasibility and usability. The selected sample consisted of 5 Italian-speaking patients with food allergy and their parents. Two medical doctor with expertise in psychology supervised the test and investigated on the eventual presence of any type of issues related to the questionnaire (e.g. clarity, culturally inappropriate expressions or difficulties in understanding the questions). The debriefing interviews included paraphrasing each questionnaire item and assessing the clarity of the

terms used and the overall understanding of the questions. Then, a group of medical doctors and psychologists discussed the feedback of the tested sample. Patients' parents had education levels ranging from middle school education to college education. Patients and parents reported that questions were simple and easy to understand and no changes were suggested. Therefore, a final spelling, grammar and formatting check was performed leading to the final approval of the first Italian version of the questionnaire. In a second phase, the questionnaire was translated into English to make it understandable and usable in other countries worldwide. The translation was carried out by two native English speakers who have not a medical background. The translations were done independently and the translators were not allowed to contact each other during the translation process. A panel of doctors compared the two versions translated into Italian which were identical for 100% of the content. This questionnaire consists of 10 items exploring several aspects of HR-QoL at T0 and any changes at T1. The questionnaire was printed and directly administered to the child. If the child had not yet acquired reading skills, the operator read the questions, and the child answered by indicating the corresponding emoticon/number [Figure 1]. The total score was expressed with a scale from 1 (best quality of life) to 3 (worst quality of life).

This questionnaire was administered to all the patients recruited in the study at the baseline (T0) and after one month (T1), directly at home, via mail, or during a follow-up visit.

To assess the feasibility and reliability of the Vitulia questionnaire, we compared our instrument with other two pre-existing questionnaires: the before mentioned FAQLQ-PF [4] and the KiddyKindl [9]. FAQLQ-PF questionnaire involves 30 items and the total score is expressed with a scale from 0 (best quality of life) to 6 (worst quality of life) [4]. KiddyKindl is a generic instrument for assessing HR-QoL in children aged 4-6 years [9]. It involves 12 items and the total score is expressed with a scale from 0 (worst quality of life) to 100 (best quality of life) [9]. Both the FAQLQ-PF and KiddyKindl questionnaires were administered at baseline and after one month. At T1, all the patients also indicated changes in their health status through a global scale of change (GSC), with a score from 0 (no change) to ± 3 (much better/worse). Clinically relevant improvement was defined as $GSC > 1$.

The aim of the validation phase was to assess the following psychometric properties:

1. Convergent validity: both at T0 and at T1, the correlation between the Vitulia score and the KiddyKindl and FAQLQ-PF scores was evaluated through the Spearman's rho correlation coefficient, considering as acceptable coefficients of about 0.5.
2. Internal consistency: both at T0 and at T1, the consistency of the questions was evaluated through the Cronbach's alpha coefficient. Values greater than 0.7 were considered acceptable.
3. Reliability was evaluated through the intra-cluster correlation coefficient (ICC) calculated on the pairs of repeated measures (T0 and T1) in children with GSC=0. The interpretation of the ICC was: low (0 to 0.20), acceptable (0.21 to 0.40), moderate (0.41 to 0.60), substantial (0.61 to 0.80), excellent (>0.80).
4. Discriminant validity was evaluated by comparing questionnaire scores in children forced to avoid 0-2 foods (average low expected score), and in those forced to avoid more than 2 foods (average high expected score).
5. Sensitivity to change (GSC>1) was assessed using the Wilcoxon rank test for paired data, applied to the mean change in scores between T0 and T1. Statistical significance was defined as a p-value <0.05.
6. Floor/ceiling effects (i.e., missing extremes in the lower/upper end of the scale) were considered present if over 15% of respondents achieved the lowest (i.e., 1) or highest (i.e., 3) possible score.

RESULTS

One hundred patients (62% male, mean age 5.4 ± 1.2 years) were enrolled. Children characteristics are shown in Table 1. No correlation was found between Vitulia questionnaire and KiddyKindl both at T0 and T1 ($p=0.305$ and $p=0.106$ respectively). On the contrary, acceptable correlations were found between the Vitulia questionnaire and the FAQLQ-PF (0.40 at T0 and 0.56 at T1, $p<0.001$) (Table 2). Cronbach's alpha coefficient for the Vitulia questionnaire total score was 0.88 at T0 and 0.89 at T1. For the “emotions” subdimension (items 1, 2, 4, 6, 7) the coefficient was 0.77 at T0 and 0.81 at

T1. For the “limitations” subdimension (items 3, 5, 8, 9, 10) the coefficient was 0.80 at T0 and 0.81 at T1 (Table 2). The ICC for the pair of repeated measures (T0 and T1) of the Vitulia questionnaire in the 23 children with GSC=0 was 0.84, with a 95% confidence interval of [0.66-0.93] (Table 2). At both visits, the average score of the new questionnaire was significantly higher in the group of children forced to avoid more than 2 foods than in those avoiding ≤ 2 foods (2.3 ± 0.5 vs 2.0 ± 0.5 and $p=0.021$ at T0; 2.3 ± 0.5 vs 2.0 ± 0.6 and $p=0.002$ at T1) [Figure 2]. Among the 46 children who reported clinically relevant improvements (GSC>1), the mean change in scores between T0 and T1 was not statistically significant (-0.05 , $p=0.364$). The lowest possible score (i.e., 1) was achieved by 2% of respondents at T0 and 3% at T1, while the highest possible score (i.e., 3) was achieved by 10% both at T0 and at T1 (no floor/ceiling effects).

DISCUSSION

The Vitulia questionnaire showed a good internal consistency along with an excellent reliability and repeatability of the measure. Another noteworthy feature of the questionnaire was its discriminant validity as demonstrated by the ability to provide different scores in subgroups, which have differences in terms of quality of life. In developing the questionnaire, we deliberately emphasized clinical features that revealed the most important aspects according to the perception of children with food allergies. We therefore identified two subdimensions: "emotions" and "limitations," for which the Cronbach's coefficient resulted in > 0.70 both at T0 and T1.

Our results supports the need for a disease-specific HR-QoL questionnaire in food allergic preschool children. The content of the Vitulia questionnaire considers the most important issues that children with food allergy have to deal with in their daily life, at school, at home or outside, impairing their HR-QoL [10]. As a result, these issues are likely to constitute significant focal points for interventions by healthcare providers, food manufacturers, and also caregivers [11]. The aim of these efforts is to enhance the quality of life for individuals with food allergies. For example items such as “Don't eat the same things as your classmates/friends” and “See classmates/friends eat all foods” have

highlighted a real discomfort in children. This finding focuses the need to raise awareness of food allergy within the community. While there have been recent improvements in labeling legislation for food-allergic patients in Europe and the USA, there has also been an increase in the use of precautionary labeling [12]. The impact of this trend on the quality of life is exemplified by the statement " Be always careful what you eat". This underscores the need to explore new therapeutic interventions that could enable children with food allergies to consume the foods they are allergic to, thereby potentially enhancing their quality of life [13].

The Vitulia questionnaire well discriminates between children who reported more than two food allergies and those who reported two or fewer. At both visits, the average score of the new questionnaire was significantly higher in the group of children forced to avoid more than 2 foods compared to those avoiding two or fewer. This finding also reflects a greater impact on the quality of life in children who experienced greater dietary restrictions, according to literature data[10].

Moreover, as we expected, significant correlations emerged between the Vitulia questionnaire and FAQLQ-PF, concerning similar relevant issues such as emotional impact and social restrictions. Unlike the FAQLQ-PF, Vitulia questionnaire investigates the most important clinical aspects related to quality of life in ten simple items and is directly administered to preschool children, who can complete it even without parental assistance. This represents a strength of our questionnaire, as children and parents differ in their opinions about quality of life. Parents are less capable of assessing symptom experiences and peer relationships from the children's perspective[14].

Nevertheless, no correlation was found with the questionnaire KiddyKindle, probably due to the generic investigation of the HR- QoL of children, unlike Vitulia, which is specific to food allergies.

Finally, our study presents some limitations. The validation process of the Vitulia questionnaire was conducted in Italian language, even though it was carefully translated into English. However, it is possible that cultural and linguistic differences may influence the questionnaire's ability to identify the most important aspects for children with food allergies [15]. Moreover, among the 46 children who reported clinically relevant improvements ($GSC > 1$), the mean change in scores between T0 and

T1 was not statistically significant, consequently the questionnaire seems not be sensitive to changes in health status over time. However, this could be due to the low reliability of using the GSC in the age group studied.

In conclusion, we presented the first self-administered disease specific HR-QoL questionnaire for children aged 4-7 years affected by food allergy. The analysis of our data suggests that Vitulia questionnaire represents a valid tool, quick and easy to interpret, which assess the most important challenges that children with food allergies encounter. The introduction of this new instrument in daily clinical practice would allow to conduct studies where assessing quality of life is the primary end-point. Examples include evaluating emerging therapies, such as oral immunotherapy and anti-IgE therapy, not only concerning the effectiveness and safety but also related to a significant reduction in the burden of the disease.

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AUTHOR CONTRIBUTIONS

GBP, SLG and LC conceived the study. AB, IP,FD and FG collected data. SF and SLG processed data. FG, SF and SP wrote the first draft of original article. GS and SP supervised the study. All authors reviewed and approved the final manuscript.

CONFLICT OF INTERESTS

The authors declare that they have no competing financial interests.

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Table 1. Characteristics of children at baseline (T0).

Age, years, no. (%)	
4	35 (35%)
5	18 (18%)
6	16 (16%)
7	31 (31%)
Gender, no. (%)	
Female	39 (39%)
Male	61 (61%)
Parent answering, no. (%)	
Mother	71 (71%)
Father	20 (20%)
Both	9 (9%)
KiddyKindl score, mean (SD)	78.3 (12.4)
FAQLQ score, mean (SD)	2.4 (1.5)
Vitulia score, mean (SD)	2.2 (0.5)
Avoided foods, no. (%)	
0-2	37 (37%)
>2	63 (63%)
Global Rating of Change (GRC, at T1)	
-3	1 (1%)
-2	0 (0%)
-1	2 (2%)
0	23 (23%)
+1	28 (28%)
+2	20 (20%)
+3	26 (26%)

SD: standard deviation.

Table 2. Convergent validity, internal consistency, and reliability of Vitulia: indicators and results.

Psychometric property	Indicator	Results
<i>Convergent validity</i>	Spearman's <i>rho</i> correlation coefficient of Vitulia and other instruments	KiddyKindl, T0: $\rho = -0.10$ ($p=0.305$) KiddyKindl, T1: $\rho = -0.16$ ($p=0.106$)
		FAQLQ, T0: $\rho = 0.40$ ($p<0.001$) FAQLQ, T1: $\rho = 0.56$ ($p<0.001$)
<i>Internal consistency</i>	Cronbach's <i>alpha</i> correlation coefficient of Vitulia	T0, total score: $\alpha = 0.88$ T0, emotions: $\alpha = 0.77$ T0, limitations: $\alpha = 0.80$
		T1, total score: $\alpha = 0.89$ T1, emotions: $\alpha = 0.81$ T1, limitations: $\alpha = 0.81$
<i>Reliability</i>	Intra-cluster correlation coefficient (ICC) for Vitulia repeated measurements (T0-T1) in children with GRC=0	ICC = 0.84 [0.66-0.93]

Figure 1. Vitulia questionnaire

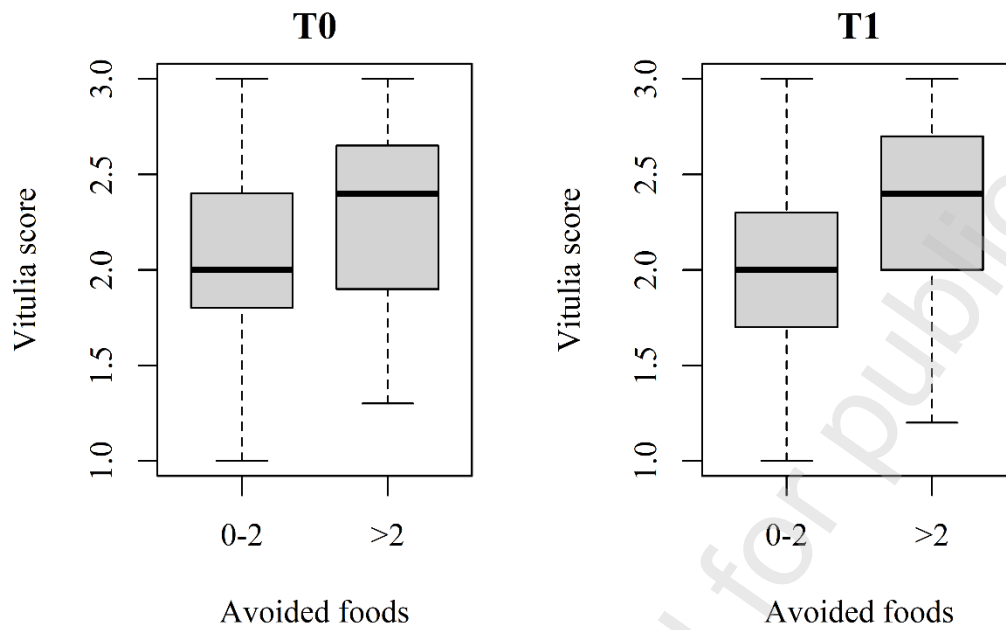


Figure 2. Discriminant validity of the Vitulia questionnaire: score distribution by number of avoided foods at baseline (T0, left panel) and after one month (T1, right panel). Boxplots represent the median (central line), 25th–75th percentiles (box), and min-max non-outlier values (whiskers).

