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Towards the Validation of the Persian Version of the Revised Cystic Fibrosis Quality of Life Questionnaire for children and parents (CFQ-R)

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Abstract

Background: The present study aimed to translate the cystic fibrosis questionnaire-revised (CFQ-R) for children with cystic fibrosis (CF) into Persian and evaluate the reliability and validity of the instrument.

Methods: About eighty individuals including children and their parents were enrolled in this cross-sectional study. Demographic characteristic and disease severity parameters of the subjects were recorded. After translation of the CFQ-R to Persian, the participants completed the parent or child translated version of the CFQ-R, as well as the PedsQL 4.0. Reliability and validity analyses were, then, carried out.

Results: The forward-backward translation was employed in this study. The total content validity ratio (CVR) and content validity index (CVI) were above 0.8 and at least 0.49, respectively. The internal reliability of each domain was acceptable (Cronbach alpha coefficients 0.65-0.91). Appropriate domains of the CFQ-R and pediatric quality of life inventory (PedsQL 4.0) were correlated, indicating the acceptable concurrent validity (r=0.5-0.7). In addition, test-retest reliability was assessed using correlation-coefficients, which were considered significant for both the child version (r=0.88; P<0.001) and parent version (r=0.78; P<0.001). Moreover, the CFQ-R scales showed significant correlations with the clinical indices and the construct of disease severity in the child and parent version.

Conclusion: According to the results, the Persian version of the child and parent CFQ-R has acceptable reliability and validity indices; and may be suggested to be used in clinical trials for the clinical evaluations and follow-ups of Iranian children with CF.

KeyWords: Child, Cystic Fibrosis, Health-related quality of life (HRQOL), Parents, Quality of Life.

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1- INTRODUCTION

A Patient-Reported Outcome (PRO) is a health outcome reported directly by patients about their health, functional status, and treatment-related quality of life. PRO Methods (PROMS) are the tools that are used in clinical settings by utilizing general or special questionnaires to report the PRO (1). PROMS are often self-report instruments, which are contributing to the quality of patient treatment and effectiveness of care (2).

Generic PRO instruments such as child health questionnaires and pediatric quality of life inventory (PedsQL4.0) generic core scales were the first questionnaires used for children (3). Although the generic health-related quality of life (HRQOL)tool evaluates multi-dimensions of health-related issues and compares treatment options for the same health condition, disease-specific HRQOL instruments have also been designed to evaluate the impact of a specific condition and its treatment on a the patients' life (4).

Cystic fibrosis (CF) is the most prevalent life-shortening disease in the Caucasian population. By improving the treatment, the survival periods have been reported to increase dramatically in recent decades (5). In this regard, the quality of life has become more important in CF patients. Multiple symptoms, associated with the disease and treatment burden, largely influence the daily life of the patients (6).

The CF questionnaire is a specific HRQOL, which has been used in several clinical trials for CF patients to measure health-related quality of life across several domains, including physical functioning, treatment burden, and respiratory symptoms (7). The instrument has three age-appropriate versions, one of which has been developed for school-age children (6-13 years), the other is for the parents of school-age children, and the final version is for adolescents and adults (aged ≥14 years) (8).

The cystic fibrosis questionnaire-revised (CFQ-R) was the final version of the CFQ which was developed by Quittner et al. with slight revisions (9).

The present study aimed to translate and psychometrically evaluate the child and parent versions of the CFQ-R.

2- MATERIALS AND METHODS

2-1. Study Population

This cross-sectional study was conducted on 80 subjects including 40 children with CF aged 6-13 years and their parents (n=40). The sample size calculation was based on power of 0.8 (power = 1 – β). To achieve the Cronbach's alpha of 0.75 for internal consistency, we needed to recruit 36 persons in each group; we raised the number to 40 for probable exclusions. The subjects were recruited from the CF clinic of Akbar Hospital, affiliated to Mashhad University of Medical Sciences in Mashhad, Iran. The CF patients aged 6-13 years who were clinically stable were enrolled in the study. They were initially asked whether they were willing to complete a quality of life measure and answer the follow-up questions. The patients and their parents who failed to complete or understand the questionnaires were excluded from the study.

Demographic characteristics and clinical parameters of disease severity (lung function test with spirometry) were collected based on standard anthropometric indices using SECA instruments for height and weight, and lung function test by spirometry indices with spirometer (CHESTGRAPH HI-105) of the included patients. The children completed the age-appropriate CFQ-R along with a general HRQOL measure, which was the PedsQL4.0 generic core scale for the measurement of the HRQOL

in children and adolescents. In addition, the parents completed the parent version of the CFQ-R. The interviewers asked the children aged 6-11 years to respond to the questions by presenting different colorful flashcards, and the selected option was pointed out by the child to the interviewer. The parents completed the appropriate questionnaires in separate rooms to avoid the possible impacts on their children's answers.

After the completion of the instruments by the patients and their parents, missing responses were eliminated by the researcher. In addition, the subjects were asked to complete the CFQ-R after two weeks if they had a stable health status in this period.

2-2. Translation

The forward translation method was initially applied for the translation of the CFQ-R into Persian by two Iranian experts (one in CF and the other with no knowledge of the disease). At the next stage, the two translations were matched, and backward translation was carried out by two native and nonnative translators. To ensure the applicability of the Persian child and parent versions, some CF patients and their parents were interviewed, and the final changes were applied to the translated versions after the interview.

2-3. Content Validity

A panel of 11 specialists and subspecialists, including gastroenterologist, nutritionist, pulmonologist, pediatrics, psychologist, experts in the field of CF responded to the questions regarding the content validity and face validity of the translated questionnaires. Lawshe's Content Validity Ratio (CVR) and the Waltz and Bausell Content Validity Index (CVI) were also used for the quantitative measurement of the translated questionnaire (10). Face validity was determined by the experts, considering the comments of the patients on the scales' assessing the desired concept, and in terms of its suitability and feasibility for the Iranian population, particularly CF patients.

2-4. Cystic Fibrosis Questionnaire (Child Version)

This questionnaire has been designed for children aged 6-13 and consists of 35 items and eight health quality domains, six of which are generic QOL (physical functioning, emotional state, social function, body image, eating disturbances, and treatment burden), and the two remaining domains are disease-specific (respiratory and digestive symptoms). The responses of the items are within the ranges of always-never and very true-very false and scored based on a four-point Likert scale. The instrument could be completed within 15-20 minutes (11).

2-5. Cystic Fibrosis Questionnaire (Parent Version)

This self-report tool was completed by the parents of children with CF regarding the quality of life of their children. The scale consists of 44 items and 11 domains; eight domains are focused on the global quality of life (physical functioning, school function, vitality, emotional state, body image, eating disturbances, weight, and treatment burden), one domain evaluates health perception, and two domains are disease-specific (digestive and respiratory symptoms). The items in this scale are scored based on a four-point Likert scale (always-never, numerous difficulties-no difficulty, and very true-very false). This instrument is completed within approximately 15-20 minutes (11).

2-6. Psychometric Evaluation

2-6-1. Internal Consistency

The internal consistency of the scales used in the present study was assessed using Cronbach's alpha, with the acceptable range considered to be 0.4-0.9 (12).

2-6-2. Test-retest Reliability

Test-retest reliability was assessed by comparing the CF scale levels between the initial test and the two-week follow-up of the children and their parents. In addition, the intraclass correlation coefficient (ICC) was performed to evaluate the reproducibility of the responses of the children and their parents.

2-6-3. Construct Validity

To measure the construct validity, correlations were examined for the CFQ-R scores in terms of the pulmonary function test, age and nutritional assessment.

2-6-4. Concurrent Validity

The PedsQL 4.0 generic core scale was utilized as a valid tool for the comparison of the CFQ-R. In addition, the correlation-coefficients were obtained for the total score and comparable domains of the CFQoL and PedsQL 4.0.

2-7. PedsQL4.0 Generic Core Scale

The PedsQL 4.0 generic core scale is a child self-report and parent proxy-report scale developed to measure HRQOL in children and adolescents aged 2-18 years. This scale consists of 23 items, which are applicable to healthy populations and patients with acute and chronic conditions. The four multidimensional scales include physical functioning (eight items), emotional functioning (five items), social functioning (five items), and school functioning (five items). The items are scored based on a five-point Likert scale (Never=0, Almost Always=4). Notably, the items are scored reversely and linearly transformed to the scale of 0-100 (0=100, 1=75, 2=50, 3=25, and 4=0). The mean score is obtained by summing up the scores of the items. The instrument could be completed within almost four minutes (13).

2-8. Statistical Analysis

Data analysis was performed in SPSS version 16 using descriptive statistics to evaluate the demographic profile and clinical characteristics of the subjects. To assess reliability, internal consistency was calculated using Cronbach's alpha. In addition, independent t-tests were applied to determine the differences in the CFQ-R scales based on the demographic and clinical characteristics. To analyze the degree of concordance between the child and parent reports, the ICCs were calculated. The coefficients below 0.4 indicated poor agreement, while those above 0.8 showed excellent agreement (14).

2-9. Ethical Considerations

The study protocol was approved by the Ethics Committee of Mashhad University of Medical Sciences, Iran (IR.MUMS.MEDICAL.REC.1399.415), and before the initiation of the study, informed consent was obtained from the parents for the enrollment.

3- RESULTS

All the participants (children and their parents) completed the questionnaires. The mean age of the children completing the CFQ-child was 8.8±2.1 years (range: 6-13 years). All the CFQ-parent respondents were mothers (100%). **Table 1** shows the Demographic characteristics of the patients.

3-1. Reliability

To determine the internal consistency, the child version of the CFQ-R was evaluated using Cronbach's alpha, which was estimated at >0.7 for all the dimensions, with the exception of social functioning (α=0.57) and respiratory symptoms (α=0.59). As for the parent version, Cronbach's alpha values of all the dimensions were >0.6, with the exception of vitality (α=0.42) and digestive symptoms (α=0.55) (**Table 2**).

Table-1: Clinical and Demographic characteristics of the patients from cystic fibrosis registry

Clinical and Demographic characteristics	value
Number of case	40
Mean Age(year)± SD (min-max)	8.8±2.1
Gender Male (Number, Percentile) Female	 17 (43%) 23 (57%)
BMI(kg/m^2); Mean± SD	11.83±23.6
BMI Z score; Mean± SD	-1.4 (1.38)
FEV1 prediction (percentage)	79.6±17.2 (mean±SD) Mild (FEV1>70%) Moderate (40≤FEV1≤70) Severe (FEV1<40%)
Sweat chloride test(meq);Mean± SD	98.2±26.24
CFTR mutation	G542X: Homozygote (2), Heterozygote (3) W1282X: Heterozygote (3) *Δ* F508: Homozygote (9), Heterozygote (2) p.Ala120Thr/p.Met952Ile (3)
Clinical manifestation	Pulmonary involvement (55%) Meconium Ileus (13%) Failure to Thrive (13%) Steatorrhea (6%) Others (13%)
Pseudomonas Infection	50%

CFTR; Cystic fibrosis transmembrane conductance regulator, BMI; Body mass index, FEV1; Forced expiratory volume is measured during the forced vital capacity test, SD; Standard deviation

Table-2: Mean and Cronbach alpha of each domain in CFQ-R child and parents' version.

Domain	Children (mean±SD)	Cronbach alpha	Parents (mean±SD)	Cronbach alpha
All patients	40	0.88	40	0.93
Physical functioning	82.14 ± 17.18	0.85	76.04 ± 16.70	0.85
School functioning	-	-	81.9 ± 19.8	0.65
Vitality		-	79.37 ± 14.97	0.42
Emotional functioning	79.3 ± 14.64	0.84	79.76 ± 13	0.72
Social functioning	62.73 ± 15.37	0.57		-
Body image	75 ± 26.28	0.90	65.8 ± 27.8	0.91
Eating problems	82.81 ± 19.11	0.80	88.46 ± 16.56	0.72
Weight	-	-	46.25 ± 25.66	Not applicable
Treatment burden	65.62 ± 21.13	0.77	63.3 ± 19	0.7
Health perceptions	-	-	78.12 ± 18.5	0.65
Respiratory Symptoms	81.25 ± 12.5	0.59	81.65 ± 14.59	0.82
Digestive symptoms	77.63 ± 21.77	Not applicable	84.16 ± 13.18	0.55

To measure the test-retest reliability, a subgroup of 22 patients with stable health and life conditions completed the questionnaires again after two weeks. The total correlation-coefficient was observed to be strongly positive in the child version (r=0.88; P<0.001) and parent version (r=0.78; P<0.001). Moreover, the correlation values of the domains were in the range of 0.6-0.8 in the parent version. In all the dimensions of the child version, the correlation values were calculated to be above 0.8.

3-2. Concurrent Validity

The comparable domains of the CFQ-R and PedsQL 4.0 were adequately correlated. The correlation-coefficient between the mean scores of the total CRQ-R and PedsQL 4.0 was found to be 0.68 in the child version (P<0.001) and 0.54 in the parent version (P=0.007). The observed correlations ranged from moderate to acceptable, including physical functioning (r=0.79; P<0.001), social functioning (r=0.47; P=0.004), and emotional functioning (r=0.60; P<0.001) in the child version of the questionnaire. In the parent version, the sequence of the dimensions was physical functioning (r=0.42; P<0.001), school function (r=0.58; P<0.001), and emotional functioning (r=0.37; P<0.02). Overall, the obtained results confirmed the concurrent validity of the CFQ-R.

3-3. Construct Validity

Body mass index (BMI) Z score, age, and disease severity were analyzed for the construct validity. Since none of the children had a severe disease; the patients were divided into two groups of normal/mild disease and moderate disease (**tables 3 & 4**). A significant correlation was observed between the total FEV1 prediction and the mean total CFQL in the parent version (r=0.48; P=0.01) and the child version of the instrument (r=0.34; P=0.02). Furthermore, the children with a mild disease achieved higher scores in all dimensions, with the exception of eating disorders. In the physical activity domain, the difference was also considered significant (P=0.02). In the parent version, the patients with more severe pulmonary diseases were observed to have a poor quality of life, especially in terms of physical activity (P=0.03), vitality (P=0.02), treatment burden (P=0.03), respiratory symptoms (P=0.001), and health perception (P=0.005).

Table-3: Gender, BMI Z score and severity of disease for known group validity in the children and parents responding CFQ-R.

	Total CFQ (parents) (mean ± SD)	Mean Difference (P-value)	Total CFQ (child) (mean ± SD)	Mean Difference (P-value)
FEV1				
<70%	67.05 ± 13.1	0.01	69.10 ± 15.26	0.14
>70%	79.8 ± 8.94		77.79 ± 11	
Gender				
Men	77.14 ± 12.47	0.29	76.13 ± 13.62	0.80
Women	72.9 ± 11.2		75.16 ± 11.32	
BMI Z-Score				
<-1 SD	68.30 ± 10.50	0.001	72.39 ± 13.37	0.11
>-1	81.43 ± 8.98		88.46 ± 10.51	

CFQ-R; Cystic Fibrosis Questionnaire-Revised, BMI; Body Mass Index

Table-4: correlation coefficients between the scale domain and the Total CFQ-R score, FEV1, age, gender, and BMI Z-Score for children and parents

	Correlation coefficient	Physical Function	Emotional Functioning	Vitality	Health Perception	Eating Disorder	Weight	Treatment Burden	Body Image	Social Function	Respiratory Symptom	Digestive Symptom
Total CFQL (children)	Pearson Correlation	0.72	0.75			0.59		0.79	0.79	0.70	0.38	0.31
	P value	≤ 0.001	≤ 0.001			≤ 0.001		≤ 0.001	≤ 0.001	≤ 0.001	0.01	0.05
Total CFQL (Parents)	Pearson Correlation	0.78	0.60	0.63	0.79	0.59	0.49	0.72	0.79	0.53	0.67	0.34
	P value	≤ 0.001	≤ 0.001	≤ 0.001	≤ 0.001	≤ 0.001	0.01	≤ 0.001	≤ 0.001	≤ 0.001	≤ 0.001	0.03
FEV1 (children)	Pearson Correlation	0.42	0.14			0.008		0.36	0.27	0.26	0.08	0.167
	P value	0.009	0.40			0.96		0.23	0.105	0.11	0.62	0.316
FEV1 (Parents)	Pearson Correlation	0.38	0.16	0.32	0.58	0.23	0.24	0.28	0.20	0.31	0.44	0.05
	P value	0.02	0.33	0.05	≤ 0.001	0.17	0.15	0.10	0.24	0.06	0.007	0.75
Age (children)	Pearson Correlation	0.11	-0.22			0.25		0.14	-0.02	-0.08	-0.16	-0.06
	P value	0.46	0.15			0.11		0.38	0.87	0.59	0.30	0.69
Age (Parents)	Pearson Correlation	-0.01	-0.11	-0.31	-0.14	-0.01	-0.21	-0.10	-0.39	0.05	-0.24	-0.14
	P value	0.94	0.47	0.05	0.38	0.91	0.18	0.53	0.01	0.74	0.13	0.38
BMI Z-Score (children)	Pearson Correlation	0.32	0.15			0.11		0.30	0.42	0.36	-0.04	0.16
	P value	0.04	0.34			0.49		0.05	0.006	0.01	0.80	0.31
BMI Z-Score (Parents)	Pearson Correlation	0.36	0.21	0.26	0.48	0.14	0.18	0.31	0.53	0.34	0.29	0.09
	P value	0.02	0.19	0.10	0.002	0.36	0.26	0.05	0.001	0.03	0.06	0.57

CFQ-R; Cystic Fibrosis Questionnaire -Revised, BMI; *Body Mass Index*, FEV1; Forced Expiratory Volume is measured during the forced vital capacity test, SD; *Standard Deviation, CFQL; Cystic Fibrosis Quality of life*

In the age comparison, only two children were aged more than 12 years, and the two age groups could not be analyzed.

The children were divided into two groups based on the BMI Z score. Malnutrition was defined as the BMI Z score of <-1. The malnourished children had a lower quality of life, especially in terms of body image (P=0.01) and social functioning (P=0.03). In addition, significant correlations were denoted between the CFQL and BMI Z score in the child version (r=37; P=0.01) and parent version of the instrument (r=0.48;P=0.001).

3-4. Agreement between Parents and Children

The assessment of agreement between the parents and children on HRQOL was performed based on the ICC. All the items had good and excellent agreement (>0.7). With regard to the domains of physical functioning and digestive symptoms, the ICC was estimated at 0.6, indicating that the parents rated the children's HRQOL to be lower in the physical functioning domain than their children, while the value was higher in the digestive symptoms domain (**Table 5**).

Table-5: Intra Class Correlation coefficients (ICC) between the children and parents in different domains of CFQ-R.

Domain	Children	Parents	ICC
Physical functioning	6	9	0.65
School functioning	-	3	-
Vitality	-	5	-
Emotional functioning	8	5	0.86
Social functioning	7	-	
Body image	3	3	0.83
Eating problems	3	2	0.77
Weight	-	1	-
Treatment burden	3	3	0.79
Health perceptions	-	3	-
Respiratory Symptoms	4	6	0.76
Digestive symptoms	1	3	0.57
Total CFQ	35	43	0.88

4- DISCUSSION

The present study aimed to translate and evaluate the psychometric properties of the CFQ-R child and parent versions in the Iranian CF patient population, and the obtained results indicated that the Persian version of the CFQ-R is a reliable and valid measure of the HRQOL for children with CF.

There are four levels of equivalence for the development and validation of quality of life questionnaires; the first level is the conception equivalence of the items with a similar meaning, the second level is the construct equivalence of subjects with different cultures and similar approaches to responding to the items, the third level involves operational equivalence regarding the same representation to the

administrators, and the final level is the metric equivalence of similar rankings along a sequence of the quality of life in different countries (21).

Conception equivalence consists of the same conceptual and semantic meaning with the basic questionnaire, as well as the qualitative assessment of the items. After the backward-forward translation in the present study, the qualitative evaluation of the items was performed based on content validity and face validity by the patients and expert panel, resulting in an acceptable scale in this regard.

In the current research, construct equivalence was evaluated using test-retest reliability and internal consistency. The acceptable correlations in all the domains in the child and parent versions provided good evidence of stability. Similarly, Quittner et al. reported acceptable ICCs in most of the domains, except for vitality, social functioning, and treatment burden (22). In the Portuguese translation, reproducibility was considered acceptable in all the domains, except for the digestive symptoms domain in the parent version and body Image in the child version (23). Considering our results and the other findings in this regard, it could be stated that the instrument is sustainable and has a strong internal reliability in all the domains, except for social functioning and respiratory symptoms in the child version and vitality and digestive symptoms domains in the parent version.

According to Quittner et al., the reliability of the tool is lower in the treatment burden and social functioning domains of the child version and the treatment burden and school functioning domains in the parent version (11). In the Turkish version, treatment burden in the child version and school functioning in the parent version had low internal consistencies (19). In the German version, lack of internal consistency has been reported in the child version for body image, social functioning, and treatment burden (17). It seems that social functioning has a low alpha coefficient in most of the studies in this regard, and it is essential to change or eliminate several items in order to increase the alpha values. In our Persian version, by eliminating the item "*You were teased by other children.*" the alpha coefficient increased to 0.62, though not reaching 0.7, yet. In the domain of respiratory symptoms, by the elimination of the item "*You had trouble breathing.*" the alpha coefficient increased to 0.61. However, no item elimination could increase the alpha coefficient for the domains of vitality and digestive symptoms in the parent version. Finally, we decided not to delete any one.

With regard to the operation equivalence, the questionnaires were designed for the young children in the age group of 6-12 years, and the adolescents in the age group of 12-13years. The CFQ-R young child version questionnaire was modified for use by an interviewer, using colorful papers (blue and orange). As for adolescents, the subjects were able to read and answer the questions on their own in a self-report manner. Finally, the metrics equivalence was evaluated based on the construct validity and ability of the CFQ-R scales to differentiate between the disease stages. To this end, the patients were categorized into two levels of disease stage based on their FEV1% predicted score. According to the obtained results, the quality of life scores were lower in those with more severe diseases, and particularly significant differences were also observed in the CFQ-R scores in the domains of physical functioning, vitality, treatment burden, respiratory symptoms, and health perception in the parent version, and physical functioning in the child version. Quittner et al. reported significant differences between the levels of the disease stage in most of the CFQ-R domains, except emotional and social functioning, and treatment burden in both

the child and parent versions (11). In a German study, children with mild diseases achieved significantly higher scores in the domains of physical functioning and respiratory symptoms in both the parent and child versions (17). According to the literature, disease severity significantly affects the quality of life of CF patients.

The prevalence of malnutrition is reported to be increased in patients with a severe genotype of CF, while patients with malnutrition have been shown to have a severe phenotype (25). In the current research, the children with malnutrition had a poor quality of life, especially in terms of the body image.

5- LIMITATIONS OF THE STUDY

Although we attempted to enroll all the eligible patients referring to the CF clinic affiliated to Mashhad University of Medical Sciences, our results might have been influenced by the small sample size. It seems that this issue could be overcome by a multicenter study across different universities. Due to the small sample size, we were not able to use factor analysis but we evaluated the validity and reliability of the questionnaire in terms of various aspects; and obtained acceptable results. Our findings could be used as a model of similar assessments regarding the quality of life of other rare genetic diseases, especially in the genetic diseases involving the gastrointestinal and respiratory tract.

6- CONCLUSION

The factors that are associated with the severity of CF, such as malnutrition and pulmonary function, directly affect the quality of life of the patients, and the CFQ-R is a reliable and valid instrument for the identification of the contributing factors to the disease outcomes.

7- CONFLICT OF INTEREST

None

8- FUNDING

None

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