

CRISTIANA FERREIRA¹ , EVA R. GOMES² , JOANA LOPES³ , SUSANA CADINHA³ 

Portuguese version of Parent-reported Drug Hypersensitivity Quality of Life Questionnaire (P-DrHy-Q): assessment of reliability and validity

¹Centro Hospitalar Tamega e Sousa, Penafiel, Guilhufe, Portugal

²Department of Allergy and Clinical Immunology, Centro Hospitalar e Universitário do Porto, Porto, Portugal

³Department of Allergy and Clinical Immunology, Centro Hospitalar Vila Nova de Gaia/Espinho, EPE, Vila Nova de Gaia, Portugal

KEY WORDS

Drug hypersensitivity; quality-of-life questionnaire for caregivers; validity and reliability; P-DrHy-Q.

Corresponding author

Cristiana Ferreira
Centro Hospitalar Tamega e Sousa
Penafiel
Avenida do Padre Americo 210
4564-007 Guilhufe, Portugal
ORCID: 0000-0003-1676-1595
E-mail: cristianasferreira@gmail.com

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Summary

Background. Drug hypersensitivity in children impacts the quality of life of the patients and their caregivers. The parent-reported drug hypersensitivity quality of life questionnaire (P-DrHy-Q), the first disease-specific quality-of-life questionnaire for caregivers who have children with drug hypersensitivity, was recently developed. The aim of this study was to assess the validity and reliability of the Portuguese version of the P-DrHy-Q. **Methods.** A translation of the Parent-reported Drug Hypersensitivity Quality of Life Questionnaire (P-DrHy-Q) to the Portuguese population was performed, assessing its applicability in 74 caregivers from two allergy departments. The analyses included internal consistency (Cronbach's alpha) and test-retest reliability: 14 caregivers completed the P-DrHy-Q without any intervention one week after answering the first questionnaire. **Results.** The 12-item scale assessed the mental health and social activity. The internal consistency of the scale was good (Cronbach's alpha = 0.884), and the test-retest associations were excellent (intra-class correlation coefficient = 0.985; $p < 0.001$). The mean value of the questionnaire was 37.01 (SD 18.57), with Mental Health being more affected than Social Activity. Employed caregivers had a significant higher score ($p < 0.001$). No other factor was statistically significant. **Conclusions.** The Portuguese version of the P-DrHy-Q is valid for evaluating quality of life impairment in Portuguese caregivers of children with drug hypersensitivity. Its application might be relevant for future research and provide clinicians and researchers with a tool to define which psychosocial support is required to provide more comprehensive care in drug hypersensitivity.

IMPACT STATEMENT

Portuguese version of the P-DrHy-Q has been developed and culturally adapted for use in Portuguese speaking population. The questionnaire may be used both in research and in routine practice in Portugal.

Introduction

Measurement of health-related quality of life (HRQoL) is critical in the global evaluation of the impacts of the diseases and their therapies (1, 2). HRQoL scales are widely used in allergic diseases as well as other chronic illnesses as an endpoint in clinical trials and in routine clinical practice (3).

These assessment measures, increasingly used, are most of the times formulated in English, targeted for its use only in the English-speaking population. Translation and cultural adaptation of health questionnaires published and applied in other cultures is important in the international setting, as they provide the use of the tool in clinical practice and in research, provide greater accuracy in measuring health aspects related to the population in question, comparison of results between different samples, as well as the cross-cultural studies.

Hypersensitivity reactions to drugs in children have a parent-reported prevalence of around 10%, with a much lower real prevalence, and a lower prevalence of confirmed DH as compared to adults (4). DHRs are considered a public health problem due to associated morbidity and socioeconomic costs.

Drug hypersensitivity may also affect the mental health and quality of life of patients and family members. The Drug Hypersensitivity Quality of Life Questionnaire was initially created by Baiardini *et al.*, and the results showed good validity, internal consistency, and reliability (5). However, measuring the quality of life in children is different from adults. Later, Yuenyongviwat *et al.* developed and validated a questionnaire for the assessment of the specific burden of drug hypersensitivity from the caregiver's perspective, using a multi-dimensional concept to examine the impact of the health status on the quality of life of caregivers who have children with a history of drug hypersensitivity: the Parent-reported Drug Hypersensitivity Quality of Life Questionnaire (P-DrHy-Q) (6).

Given the absence of specific assessment tools designed for evaluating the quality of life in caregivers who have children with drug hypersensitivity in Portugal, the main objective of this study was to develop and assess the validity and reliability of a Portuguese version of Parent-reported Drug Hypersensitivity Quality of Life Questionnaire (P-DrHy-Q). The secondary objectives were to evaluate P-DrHy-Q in different caregivers and patients' subgroups (drug hypersensitivity, type of reaction, age, single or multiple drug hypersensitivity reactions and sociodemographic of the caregivers).

Materials and methods

Ethics

The research project was approved by the Ethics Committee and carried out in accordance with the Declaration of Helsinki. All participants gave their oral informed consent to participate.

Study design and subject

Study participants were prospectively recruited from two different Allergy and Clinical Immunology Department located in tertiary healthcare centers in North of Portugal between June to July 2020. The inclusion criteria were an age under 18 years and having objective symptoms compatible with drug hypersensitivity suspicion. Medical records were scrutinized by the investigators, to determine eligibility. Parents of eligible children were invited to participate. Parents were asked to fulfill the questionnaire, and instructions were given by the investigators on how to proceed. Sociodemographic and clinical characteristics of the children and caregivers were recorded.

Parent-reported Drug Hypersensitivity Quality of Life Questionnaire (P-DrHy-Q)

P-DrHy-Q which was originally developed in Thailand includes 12 items evaluated on a ten-point Likert scale (from 1 (not at all) to 10 (many)), investigating two different domains: Mental Health and Social Activity (6). It was designed to be completed by the caregiver, it is easy to administer and to score and requires a few minutes to complete. Questions and scores were formulated so that higher scores reflected worse HRQoL.

Translation and cross-cultural adaptation methods

The process of linguistic equivalence was initiated by contacting the authors of the original questionnaire to ask for authorization to use it in the present study. Cross-cultural translation was performed according to guidelines (7). Linguistic validation consisted in 3 steps: forward translation, backward translation and comprehensibility testing. Forward translation was performed by two independent translators that had no previous knowledge of the questionnaire. Both were native speakers in the target language. Supported by an experienced specialist in drug allergy diagnosis and treatment, a combined version was obtained. Agreement was achieved through unanimity on a single reconciled version with all elements (translators and physician). The consensual version was tested in caregivers of children with a history of drug hypersensitivity. No comments, doubts or suggestions were posed, showed that the questions were easily understandable and do not require explanation.

Reliability

Reliability measures were of two types: 1) Internal consistency was evaluated using Cronbach's alpha calculated for each scale, and 2) Test-retest reliability (reproducibility). P-DrHy-Q was administered twice to 14 caregivers separated by 7 days interval in the absence of any significant clinical or personal change; intraclass correlation coefficients quantified reproducibility of scores over 7 days.

Statistical analysis

SPSS version 22 (SPSS-Inc, Chicago, IL) was used for statistical analysis. Quantitative variables were expressed as means \pm

standard deviations, with 95% confidence intervals. Qualitative variables were compared using χ^2 test and Fisher's exact test. The normality was verified using the Shapiro-Wilk test. For all variables, significance was set at $p < 0.05$ for two tails. The internal consistency of the scale was evaluated using Cronbach's alpha coefficient. It is accepted crossways that $\alpha > 0.7$ is acceptable, > 0.8 is good, and > 0.9 is excellent. Intra-class correlation coefficient was performed to assess the discriminative reliability of the test-retest associations.

Results

In the cognitive debriefing no comments, doubts or suggestions were done.

Characteristics of the participants

There were no refusals to participate in the study. A total of 74 caregivers with a child with a reliable history of drug hypersensitivity were included in this study.

Demographic characteristics of the patients were shown in **table I**: 48.6% ($n = 36$) of the children were females and 51.4% ($n = 38$) were males. Ages ranged from 1-15 years with an average of 5.08 ± 3.64 years. Mild reactions in 85.1% ($n = 63$) of cases, moderate 9.5% ($n = 7$) and severe 5.4% ($n = 4$) were observed. The most common implicated drugs to hypersensitivity reactions were antibiotics (65/74 patients, 87.8%) and non-steroidal anti-inflammatory drugs (5/74 patients, 6.8%) and 2 (2.7%) had a history of drug hypersensitivity reaction to more than one drug.

Demographic characteristics of the caregivers were shown in **table II**: 86.5% ($n = 64$) were female and 13.5% ($n = 10$) were male. Their ages were ranged from 30-45 years in 74.3% ($n = 55$), 20-30 years in 16.2% ($n = 12$) and over 45 years in 9.5% ($n = 7$). 47.3% ($n = 35$) had basic education, 27.0% ($n = 20$) university graduation. 78.4% ($n = 58$) were employed and 21.7% ($n = 16$) unemployed. 89.2% ($n = 66$) were married and 98.6% were the main caregiver. Most of the family income was above 600 euros (€)/month. None of them have previous experienced in care of children with drug hypersensitivity.

The average global score was 37.01 (0-120), mean Mental Health 27.92 ± 13.66 (0-50; questions 1-5) and Social Activity 9.09 ± 6.34 (0-70; questions 6-12) (**table III**). The Mental Health presented higher scores than social that indicate that is the domain more affected in the caregivers.

There were no statistically significant differences in the scores between the clinical characteristics of the patients (sex, age, severity of the reaction or number of drugs involved). However, in regard to sociodemographic characteristics of the caregivers, it was found that when the caregiver is employed, the Social Activity Score is higher compared to unemployed cases (**table IV**).

Table I - Demographic and clinical characteristics of the children.

	n (%)	Mean \pm SD
Gender		
Female	36 (48.6%)	
Male	38 (51.4%)	
Age		5.08 \pm 3.64
Reaction severity		
Mild (urticaria, maculopapular exanthema, eczema)	63 (85.1%)	
Moderate (angioedema, serum-like disease, dyspnea, vomits)	7 (9.5%)	
Severe (generalized exfoliative dermatitis, erythroderma, cutaneous vasculitis, bullous eruptions, DRESS, NET/SJS)	4 (5.4%)	
Drug class		
Antibiotic	65 (87.8%)	
B-Lactamic	61 (82.4%)	
Others	4 (5.4%)	
NSAIDs	5 (6.8%)	
Anticonvulsants	1 (1.4%)	
Psychotropic drugs	3 (4.1%)	
Number of drugs		
1	72 (97.3%)	
> 1	2 (2.7%)	

Reliability

The P-DrHy-Q showed adequate internal consistency, as demonstrated by the very strong Cronbach's alpha coefficient ($C = 0.884$). In **table V**, the values represented are the Cronbach's alpha coefficient of the scale if that question were excluded. Mental Health and Social Activity subscales were also adequate: $C = 0.988$, $p < 0.001$; and $C = 0.997$, $p < 0.001$, respectively (**table VI**).

Test-retest reliability was assessed on 14 caregivers and was excellent: ICC = 0.985, $p < 0.001$ (**table VI**) for scales, but also in Mental Health and Social Activity subscales: ICC = 0.978, $p < 0.001$ and ICC = 0.992; $p < 0.001$ respectively (**table VI**).

Discussion

Evaluation of patient-reported outcomes by validated tools, either disease-specific when available or generic ones, in clinical trials for allergic diseases are very important. An original questionnaire allowing the assessment of impact of biopsychosocial

Table II - Sociodemographic characteristics of the caregivers.

	n (%)
Sex	
Female	64 (86.5%)
Male	10 (13.5%)
Current age	
20-30 y	12 (16.2%)
30-45 y	55 (74.3%)
> 45 y	7 (9.5%)
Main caregiver	
No	2 (1.4%)
Yes	72 (98.6%)
Marital status	
Married	66 (89.2%)
Divorced	2 (2.7%)
Single	6 (8.1%)
Occupation	
No	16 (21.7%)
Yes	58 (78.4%)
Education	
Basic	35 (47.3%)
Technological	7 (9.5%)
University graduation	20 (27%)
Master's	10 (13.5%)
Doctorate	2 (2.7%)
Number of children within family	
1-2	65 (87.6%)
2-4	9 (12.2%)
Family income, euros (€)/month	
< 600	3 (4.1%)
600-1,500	35 (47.3%)
1,500-3,000	18 (24.3%)
> 3,000	18 (24.3%)
Previous experience in care of children with drug hypersensitivity	
No	74 (100%)
Yes	0 (0%)

factors on drug allergy in caregivers of drug hypersensitivity pediatric patients entitled P-DrHy-Q has recently been developed and validated (6). The original version was primarily developed in English language. In the present study this tool was trans-

Table III - Total scores for the P-DrHy-Q and subscales.

Scores	Total (n = 74) Mean ± SD
Total	37.01 ± 18.57 [0-120; questions 1-12]
Mental Health	27.92 ± 13.66 [0-50; questions 1-5]
Social Activity	9.09 ± 6.34 [0-70; questions 6-12]

lated and culturally adapted to Portuguese speaking population. To our best knowledge, our study is the first that validates P-DrHy-Q for another language and culture after development of the original questionnaire. Cross-cultural adaptation is relevant because, currently, there is no other measure for quality of life of caregivers with drug hypersensitivity children in Portugal. The decision to culturally adapt the P-DrHy-Q, rather than to develop a new measure, was based on the fact that the adaptation of a previously described and validated measure, which has been translated and validated to other languages, makes it possible to compare results across studies conducted in different countries. This present study contributes to attain this gap, both in clinical trials and in routine practice.

The results of the study showed that the P-DrHy-Q is a self-applied psychosocial impact scale in drug allergy. Furthermore, it is a brief and low-cost way to assemble data that may guide the clinician to decide which factors should be included in a multidisciplinary approach to the caregivers. The factor analysis demonstrated that the scale may be used to measure two types of parental burden: mental health and social activity. Both of these domains had excellent internal reliability in both versions of the scale. The statistical analyses provided evidence that Portuguese version of the P-DrHy-Q met the standards for good internal consistency reliability with a Cronbach's alpha of $R = 0.884$, $p < 0.001$ along with excellent test-retest reliability, ICC = 0.985 (Thailand version: Cronbach's alpha = 0.897 and the test-retest reliability, ICC = 0.9439, $p < 0.001$). Therefore, it may be possible to adapt the scale to incorporate two sub-scale scores as well as an overall score to provide more information on the type of parental burden that is most salient.

The average score of P-DrHy-Q in our 74 for caregivers of patients who had suffered an allergic reaction with a drug were 37.01 ± 18.57 . Its application demonstrated negative impact on mental health and social activity in the caregivers of affected children. In our study we found higher score in the mental score than the social.

We believe that our study had some strengths. The study was performed in two different Allergy and Clinical Immunology Department and includes patients with different types of drug allergy.

Table IV - Item-scale correlations on the P-DrHy-Q.

	Score Total	Mental Health	Social Activity
Patients			
Gender			
Female			
Male	0.828	0.894	0.727
Age		0.691	0.930
Severity of the reaction			
Mild			
Moderate	0.232	0.401	0.077
Severe			
Number of drugs			
1			
> 1	0.788	0.802	0.806
Caregivers			
Sex			
Female			
Male	0.492	0.493	0.593
Current age			
20-30 y			
30-45 y	0.201	0.222	0.259
> 45 y			
Main caregiver			
No	0.677	0.996	0.217
Yes			
Marital status			
Married			
Divorced	0.632	0.828	0.263
Single			
Occupation			
No			
Yes	0.182	0.370	0.001*
Education			
Basic			
Technological			
University graduation	0.515	0.302	0.981
Master's			
Doctorate			
Number of children within family			
1-2			
2-4	0.571	0.523	0.775
Family income, euros (€)/month			
< 600			
600-1,500			
1,500-3,000	0.605	0.604	0.608
> 3,000			

Table V - Mean score, squared, minimum and maximum value, multiple correlations, and Alpha Cronbach if item deleted, for each question of the P-DrHy-Q.

	Mean	Standard deviation	Min; max	Multiple correlation	α Cronbach if excluded
Mental Health					
1. O seu sono alterou devido à alergia aos medicamentos do seu filho? [Did you have sleep disorder problem due to your child's drug allergy?]	2.86	2.6	1; 10	0.758	0.871
2. A alergia aos medicamentos do seu filho afetou seu humor? [Did your child's drug allergy affect your mood?]	2.78	2.63	1; 10	0.740	0.871
3. Esteve preocupado/a que a possibilidade do seu filho vir a ter outra reação alérgica aos medicamentos? [Were you worried that your child will be allergic to drug again?]	6.97	2.83	1; 10	0.569	0.873
4. A preocupação do seu filho ter outra reação alérgica aos medicamentos afetou-o/a? [Would the worry of your child allergic to drug again affected you?]	4.49	2.80	1; 10	0.704	0.867
5. O medo do seu filho ter outra reação alérgica a medicamentos afetou-o/a? [Would the fear of your child allergic to drug again affected you?]	5.22	2.95	1; 10	0.760	0.867
6. Receia que o seu filho venha a ter dificuldades de aprendizagem devido à sua alergia aos medicamentos? [Did you worry that your child would have a learning problem due to drug allergy?]	1.95	1.92	1; 10	0.531	0.877
7. A alergia aos medicamentos do seu filho deixou-o/a frustrado/a? [Did your child's drug allergy make you frustrated?]	3.65	2.85	1; 10	0.338	0.884
Social Activity					
8. Preciso de cuidar do seu filho mais do que o habitual nas saídas com ele? [Did you needed to take care of your child more than usual when you go out?]	2.62	2.62	1; 10	0.842	0.861
9. A alergia aos medicamentos do seu filho fez com que não tivesse tempo para as suas atividades de lazer (desporto, ler um livro, ver um filme, refeições fora)? [Did you have time for leisure activities (exercise, movie, eating out) although your child's drug allergy?]	1.74	1.63	1; 10	0.653	0.877
10. A alergia aos medicamentos de seu filho fez com que ele se sentisse diferente das outras crianças? [Did your child's drug allergy make him/her feel discriminated?]	1.5	1.21	1; 7	0.417	0.886
11. A alergia aos medicamentos do seu filho afetou o orçamento da sua família? [Did your child's drug allergy affect your family budget?]	1.74	1.54	1; 8	0.284	0.882
12. A alergia aos medicamentos do seu filho afetou as suas interações sociais? [Did your child's drug allergy affect your social interactions?]	1.49	1.35	1; 8	0.522	0.880

Square brackets: translation of the questions for Journal's readers.

Table VI - Internal consistency and test-retest reliabilities of the P-DrHy-Q Scale and subscales.

	Number of items	Cronbach's alphas	ICC
Total scale P-DrHy-Q	12	0.884	0.975
Subscales			
Mental Health	7	0.988	0.978
Social Activity	5	0.997	0.992

Second, we had opportunity to observe relationship of the P-DrHy-Q scores to other clinical factors of the patients and sociodemographic characteristics of the caregivers. In the process of validating the DrHy-Q questionnaire, Baiardini *et al.* found that the highest score (and therefore worse QoL) occurred in patients who had suffered anaphylaxis (5). Results of our study showed that the group of caregivers employed had significantly higher P-DrHy-Q scores, in particular Social Activity Score, indicating a worse HRQoL compared to unemployed individuals, which can be explained due to a more stressful life in the employed caregivers and less time available to control situation to less control in child diary activity. No other statistically significances were found.

This study has also several limitations. Our study has a small sample size; the analysis of a greater number of cases may reveal more robust results.

Other limitation of the study was that it does not takes into account the influence of a drug allergy evaluation and does not analyze if the quality of life improved significantly after completing a drug allergy evaluation. Gatamintza *et al.* conducted a prospective multicenter study in Spain to evaluate the quality of life of patients who suffered a possible allergic drug reaction, and analyzed the effect of a drug allergy evaluation (8). A total of 346 adult's patients answered the specific questionnaire twice: before the drug allergy evaluation, and 1 month after it was completed. The quality of life was found to be significantly improved after completing a drug allergy evaluation.

The Portuguese version of the P-DrHy-Q has been developed and culturally adapted for use in Portuguese speaking population. This is the first parent-reported health-related quality of life instrument for drug allergy. This study demonstrated that the Portuguese version of the P-DrHy-Q can be a tool to evaluate interaction of biopsychosocial factors in caregivers of drug hypersensitivity patients. It shows good internal consistency and reliability. The questionnaire may be used both in research and in routine practice in Portugal. Gaining information on which type of parental burden is more salient provide more comprehensive care in drug hypersensitivity and may be useful in determining appropriate support for the caregivers.

Fundings

None.

Contributions

CF, EG, JL, SC: study design, writing – original draft, writing - review & editing. CF: results interpretation.

Conflict of interests

The authors declare that they have no conflict of interests.

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