Adaptation and Validation of the Israeli Version of the Chronic Urticaria Quality of Life Questionnaire (CU-Q2oL)

Aharon Kessel MD[1], Yael Graif MD[2], Zahava Vadasz MD[1], Vered Schichter-Konfino MD[1], Meital Almog MD[1], Shai Cohen MD[3], Valery Teplitski MD[2], Nili Stein MPH[4], Ilaria Baiardini PhD[5], Marcus Maurer MD[6] and Elias Toubi MD[1]

[1]Division of Allergy and Clinical Immunology, Bnai Zion Medical Center, affiliated with Rappaport Faculty of Medicine, Technion-Israel Institute of Technology, Haifa, Israel
[2]Allergy and Immunology Clinic, Pulmonary Institute, Rabin Medical Center (Beilinson Campus), Petah Tikva, affiliated with Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel
[3]Division of Internal Medicine and [4]Department of Community Medicine and Epidemiology, Carmel Medical Center, affiliated with Rappaport Faculty of Medicine, Technion-Israel Institute of Technology, Haifa, Israel
[5]Allergy & Respiratory Diseases Clinic, DIMI, University of Genoa, IRCCS AOU San Martino-IST, Genoa, Italy
[6]Department of Dermatology and Allergy, Allergie-Centrum-Charité/ECARF, Charité-Universitätsmedizin, Berlin, Germany

ABSTRACT: **Background:** Chronic urticaria (CU) is a common disabling disorder. The CU-Q2oL (Chronic Urticaria Quality of Life Questionnaire) is a specific questionnaire for evaluating quality of life in CU patients. It consists of 23 items divided into six quality-of-life dimensions. It was initially developed in Italy and later validated in other countries.

Objectives: To validate and adapt the CU-Q2oL to the Hebrew language in order to make it suitable for use in Israel.

Methods: The CU-Q2oL questionnaire was translated to Hebrew. A group of 119 CU patients were asked to complete this version, in addition to the Dermatology Life Quality Index (DLQI) and Urticaria Activity Score (UAS) questionnaires. A factorial analysis was performed to identify CU-Q2oL subscales, internal consistency and convergent validity assessment, as well as factors determining quality-of-life scores.

Results: The factor analysis identified six scales of the Israeli CU-Q2oL: (i) sleep and concentration, (ii) function and mental status, (iii) embarrassment and clothing limitations, (iv) itching, (v) eating behavior and medication side effects, and (vi) swelling, which accounted for 77% of the data variance. Five scales showed good internal consistency over 0.81. The mean ± SD score of CU-Q2oL in our patients with CIU was 41 ± 21.7. We found a strong positive correlation between the overall scores of CU-Q2oL and DLQI questionnaires ($r = 0.8$, $P < 0.01$). Additionally, we found a positive correlation between UAS and both CU-Q2oL and DLQI ($r = 0.62$, $P < 0.01$, and $r = 0.53$, $P < 0.01$, respectively).

Conclusions: This study demonstrates that the Israeli CU-Q2oL questionnaire is suitable for both clinical use and research in Israel.

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KEY WORDS: chronic urticaria (CU), quality-of-life questionnaire, Chronic Urticaria Quality of Life Questionnaire (CU-Q2oL), adaptation, validation

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Chronic urticaria (CU) is a common disabling disorder, occurring in 0.5–1% of the population, with an average duration of 3–5 years in adults [1]. In a previous study conducted in Israel, CU persisted for more than 1 year in over 70% of patients. After 36 months of follow-up 43% of patients were still suffering from CU, and after 5 years – when the study ended – 14% of patients were still suffering [2]. The impact of CU on patients' quality of life (QoL) is often underestimated. O'Donnell et al. [3] showed that health status scores of patients with CU are comparable to those of patients with coronary artery disease. Understanding the effects of CU on the QoL of affected patients is critical for both optimal management and clinical research. Therefore, QoL should be included as an outcome measure in clinical trials that assess the overall effectiveness of treatment. In the past, the QoL of CU patients was assessed by generic questionnaires applicable to all health conditions, and by a specialty-specific questionnaire developed for skin diseases. In this respect, Baiardini et al. [4] developed a specific questionnaire for evaluating QoL in CU patients. This questionnaire, called the Chronic Urticaria Quality of Life Questionnaire (CU-Q2oL), has been validated, including the physical, emotional, social and practical aspects that characterize this disease. In different countries, such as Germany, Spain and Turkey, CU-Q2oL was translated to the local language and was found to meet the standards for validity, internal consistency, reliability and responsiveness [5-8]. The aim of the present study was to validate and adapt the CU-Q2oL to the Hebrew language in order to make it suitable for use in Israel.

PATIENTS AND METHODS

Patients over 18 years old with chronic spontaneous urticaria who visited the allergy outpatient clinic of Bnai Zion Medical

Table 1. English version of the CU-Q_2oL questionnaire

Item no.	Item name	Question
1	Pruritus	Itching
2	Wheals	Wheals
3	Eye swelling	Swelling of your eyes
4	Lip swelling	Swelling of your lips
5	Work	Work
6	Physical activities	Physical activities
7	Sleep	Sleep
8	Free time	Free time
9	Social relationships	Social relationships
10	Eating	Eating
11	Falling asleep	Do you have difficulties falling asleep?
12	Waking up	Do you wake up at night?
13	Tired	Are you tired during the day, because you didn't sleep well at night?
14	Concentration	Do you have difficulties concentrating?
15	Nervousness	Do you feel nervous?
16	Bad mood	Do you feel miserable?
17	Food limitations	Do you have to limit your food choices?
18	Bothered by signs	Are you bothered by the symptoms of hives that appear on your body?
19	Embarrassed in public	Are you embarrassed to go to public places?
20	Cosmetics	Is it a problem for you to use cosmetics (e.g., perfumes, creams, lotions, bubble bath, make up)?
21	Clothing	Do you have to limit your clothing choices?
22	Sports	Are your sports activities limited because of your hives?
23	Medication side effects	Do you suffer side effects from the medications you take for hives?

In the table the English version is shown, along with a shortened name. Each statement or question is scored on a 5-point scale; namely, responders specify their level of agreement or disagreement on a symmetric agree–disagree scale for a series of questions

Table 2. Composition and internal consistency of the Israeli version of the CU-Q_2oL questionnaire subscales

	No. of questions	Question no.	Cronbach's α coefficient
Factor I (Sleep, concentration)	5	7, 11, 12, 13, 14	0.92
Factor II (Functioning, mental status)	7	5, 6, 8, 9, 15, 16, 22	0.91
Factor III (Embarrassment, clothing limitations)	4	18, 19, 20, 21	0.81
Factor IV (Itching)	2	1, 2	0.89
Factor V (Eating behavior, medication side effects)	3	10, 17, 23	0.71
Factor VI (Swelling)	2	3, 4	0.83

Center (Haifa, Israel) and Rabin Medical Center (Petah Tikva, Israel) were invited to participate in this study. The study was approved by the Helsinki Ethics Committee in both participating centers.

After signing an informed consent the patients were asked to complete the study questionnaires. The questionnaire packages were provided personally in all cases during visits to our outpatient clinics. Data were collected from April 2013 until January 2014.

TRANSLATION OF THE QUESTIONNAIRE

The original Italian version was translated into Hebrew by a professional Israeli translator trained in medical translation. The translation was performed by using the forward and back-translation procedure. Before starting the study, this translation was approved by several expert allergists for the comprehensibility of the items.

CU-Q_2OL QUESTIONNAIRE

The CU-Q_2oL is a 23-item health-related QoL (HRQoL) questionnaire that was originally developed in Italy [4]. It measures six dimensions (scales) of HRQoL: pruritus (2 items), swelling (2 items), impact on life activities (6 items), sleep problems (5 items), limitations (3 items), and appearance (5 items). Items are answered on a 5-point Likert-type scale. The scores of the scales are calculated by using linear transformations of raw scores; the minimum and maximum possible scores are 0 and 100 respectively for each scale, with 100 indicating the worst HRQoL.

THE DERMATOLOGY LIFE QUALITY INDEX (DLQI)

The DLQI was designed to provide a quick simple assessment of QoL for routine clinical use [9,10]. The DLQI consists of 10 questions, each relating to a different aspect of skin disease. Individual questions are scored from 0 to 3 according to the grading: not at all, a little, a lot, or very much, with high scores representing a poor quality of life. The total score ranges from 0 to 30.

URTICARIA ACTIVITY SCORE (UAS)

The UAS is a validated scoring system combining the intensity of itch and the number of wheals culminating in a score between 0 and 6. Patients are instructed to record the severity of their itch and the number of hives twice a day – morning and evening. [11]. As it is advised by the European Academy of Allergology and Clinical Immunology, Global Allergy and Asthma European Network, European Dermatology Forum, and World Allergy Organization (EAACI/GA2LEN/EDF/WAO) to document patient's self-perception score for several days, the patients in our study were instructed to fill in their average score regarding itch severity and hive number during the 2 weeks before the clinic visit. Questions in the CU-Q2oL questionnaire also relate to symptoms in the 2 weeks before the clinic visit.

STATISTICAL ANALYSIS

Statistical analysis was performed using IBM Statistics (SPSS) vs. 21. The continuous variables were presented by mean and standard deviation. The categorical variables were presented in percentages. Exploratory factor analysis was used to determine the potential subscales with proper item division of the translated new Israeli questionnaire version of CU-Q2oL. Using Varimax factor rotation with Kaiser normalization, data were reduced to summary scores. The criterion chosen to retain factors was an Eigenvalue ≥ 1.0 for that factor. Individual items were assigned to the factor when loading with a factor loading ≥ 0.5. After identifying the scales, Cronbach's correlation coefficient was calculated for each scale to test its internal consistency. Correlations between two continuous variables were analyzed using Pearson or Spearman correlation as appropriate. Correlations of < 0.40, 0.40–0.60 and > 0.60 were defined as weak, moderate and strong, respectively [13]. Differences between gender scores were analyzed using the independent *t*-test. $P < 0.05$ was considered statistically significant.

RESULTS

The study group comprised 119 patients (81 females and 38 males, 68.1% and 31.9% respectively) with an age range of 44.23 ± 15.0 years (mean age ± standard deviation). Since a minimum sample size of five subjects per variable is recommended [5], this group size was adequate for factor analysis. The mean duration of disease was 23.0 ± 36.7 months. Almost one-third (32.6%) of the patients had, in addition to chronic spontaneous urticaria, physical urticaria. Forty-six of 97 patients (47.5%) also had angioedema.

CU-Q$_2$oL QUESTIONNAIRE

The translation of the original Italian questionnaire to English is shown in Table 1. In order to validate the questionnaire, we performed factor analysis which yielded a six-factor solution for the Israeli data. We then assessed the internal consistency of these six scales, as calculated by Cronbach's correlation coefficient. The values of all the dimensions exceeded the minimum reliability standard of 0.50–0.70 recommended for group comparison [Table 2].

QUALITY-OF-LIFE SCORES

The mean score of CU-Q$_2$oL of our patients with CIU was 41 ± 21.7 (mean ± SD). The most affected scales were Factor IV (itching) and Factor I (sleeping and concentration), while Factor V (eating and medication side effects) (7.69 ± 5.5) was the least affected. The median and mean scores, respectively, of the scales are detailed in Table 3. Regarding gender differences, CU-Q$_2$oL scores of women were affected more than those of men (44 ± 20.9 vs. 34.8 ± 22.4, $P = 0.032$). Additionally, women suffered more than men in a few subscales, such as itching (Factor IV) (69 ± 27 vs. 58 ± 31, $P = 0.04$), swelling (Factor VI (34 ± 30 vs. 21 ± 24, $P = 0.025$), and embarrassment/clothing limitations (Factor III) 40 ± 26 vs. 26 ± 25, $P = 0.007$).

Table 3. Chronic Urticaria Quality of Life Questionnaire (CU-Q$_2$oL) subscales scores and CU-Q$_2$oL total score in the examined population

	No.	Mean	Median	SD	Minimum	Maximum
Factor I	119	48.78	45.00	29.18	0.00	100.00
Factor II	119	42.13	39.28	27.38	0.00	100.00
Factor III	119	36.18	31.25	27.03	0.00	100.00
Factor IV	119	66.28	75.00	28.86	12.5	100.00
Factor V	119	7.69	5.55	8.00	0.00	33.33
Factor VI	119	29.83	25.00	29.34	0.00	100.00
Total factor grade	119	41.08	39.1	21.7	2.17	96.74

SD = standard deviation

DLQI QUESTIONNAIRE

The mean grade for the DLQI questionnaire was 34.77 ± 25.1.

URTICARIAL SEVERITY QUESTIONNAIRE

We then correlated the scores of CU-Q$_2$oL, DLQI and UAS. We found a strong positive correlation between the overall scores of the CU-Q$_2$oL and DLQI questionnaires ($r = 0.8$, $P < 0.01$) [Figure 1A]. In addition, we found a statistically positive correlation between UAS and CU-Q$_2$oL ($r = 0.62$, $P < 0.01$) [Figure 1B]. A positive correlation was also found between the DLQI and the UAS questionnaires ($r = 0.53$, $P < 0.01$).

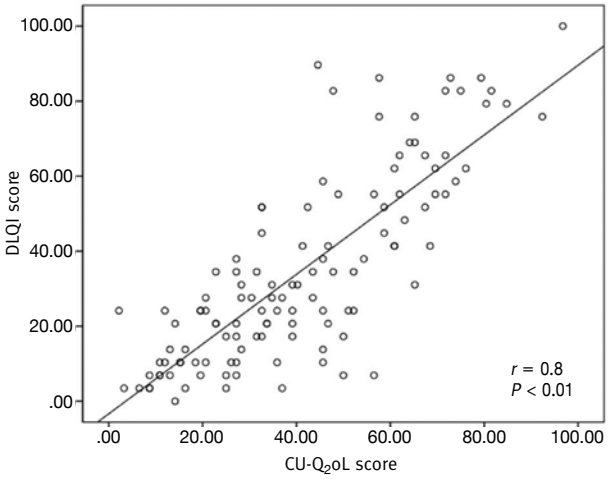
OTHER CORRELATIONS

We did not find any correlation between disease duration or age and global mean scores of the CU-Q$_2$oL questionnaire or with the different subscales of the CU-Q$_2$oL questionnaire.

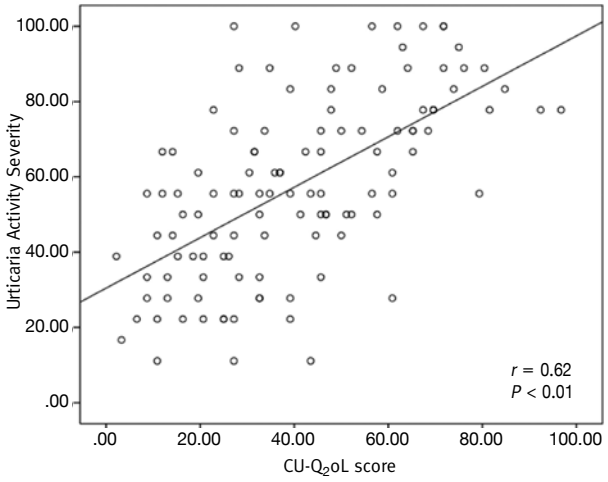
DISCUSSION

One of the recommendations of the Global Allergy and Asthma European Network (GA^{2}LEN) is to find a universal quality-of-life questionnaire that is applicable to all CU patients around the world in their own language. When evaluating QoL in a clinical trial, the physician must choose between a generic and a disease-specific questionnaire. Since generic measures are designed for general populations, they are less likely to identify small but clinically important changes induced by treatment. Thus, the CU-Q$_2$oL includes items that are likely to be specific for chronic urticaria. It is expected that the CU-Q$_2$oL will provide the physician with a better questionnaire than the generic to detect clinical changes and, therefore, is more appropriate for clinical trials designed to assess responses to therapy or to compare between different treatments.

Figure 1. [A] Correlation between the Chronic Urticaria Quality of Life (CU-Q_2oL) questionnaire and the Dermatology Life Quality Index (DLQI) questionnaire. Each dot represents one patient. The correlation between the DLQI total score and CU-Q_2oL total score was statistically significant ($P < 0.01$, r (Pearson) = 0.8)



[B] Correlation between the Chronic Urticaria Quality of Life (CU-Q_2oL) questionnaire and the Urticaria Activity Score (UAS). Each dot represents one patient. A positive correlation was found between the CU-Q_2oL total score and UAS ($P < 0.01$, r (Pearson) = 0.62)



We found the Israeli version of the CU-Q_2oL to be a reliable and valid instrument for use in Israeli chronic urticaria patients. It is simple to use, non-time consuming and in our experience can be filled in 5–10 minutes.

The results of our factorial analysis were quite satisfying as the analysis allowed us to retain all the items. It resulted in a six-factor solution explaining > 77% of variance, proving its strong validity. Factor solution in the Italian CU-Q_2oL was almost 60%, whereas the German version explained > 70% of variance.

We recognized six subscales with satisfying face validity. Factor I (Sleep subscale) consists of five items explicitly related to sleeping problems. Factor II (Functioning/Mental status subscale) combines mental items and items related to daily activities. Factor III (Embarrassment/clothing limitations subscale) consists of four items that combine the patient's embarrassment from urticaria symptoms such as wheals, pruritus or swelling with factors concerning limitations in choice of clothes and use of cosmetics. Factor IV (Itching subscale) includes two items that regard pruritus and wheals as related to each other. Eating behavior and medication side effects are included in the Factor V subscale. This finding can be explained by the notion that the Israeli patients were less affected by medication side effects and food limitations as this subscale got the lower grade [Table 3]. Factor VI (Swelling subscale) contains two items related to swelling. We found that Itching (Factor IV) was the most impaired subscale. The same results were obtained in previous studies performed in German, Turkish, Spain and Polish CU patients [5-8]. This finding was expected since pruritus is the prominent and particularly debilitating symptom in urticaria and the main factor in the urticarial severity questionnaire.

We found that the sleep problems and concentration subscale was the second highest affected factor. This is not surprising since a nationwide internet survey on CU patients from Germany and France revealed widespread sleep disturbances [14]. It makes clinical sense that sleep problems are related to concentration difficulties. The medication side effects (Factor V) scored as the lowest affected subscale due to the fact that most of our patients were treated with second-generation non-sedating antihistamines.

In terms of reliability, the Israeli version of the CU-Q_2oL performed well in the present study, with Cronbach-α values over the recommended 0.70 threshold in all the dimensions and for the overall score. Internal consistency results were generally comparable with, or better than, those seen for the original instrument.

Since chronic spontaneous urticaria is a fluctuating disease, its activity can change significantly over time without any medical therapy. On the other hand, symptomatic treatment can also modify disease activity and severity. Hence, it is important to have available patient-reported outcomes that are able to mirror these changes both in clinical studies and in routine care. In particular, we found that the CU-Q_2oL questionnaire was able to differentiate patient groups with different degrees of urticaria activity. We found a high statistically positive correlation between disease activity (UAS score) and CU-Q_2oL total score ($r = 0.62$, $P < 0.01$). Therefore, the higher the disease activity, the higher the QoL impairment found by the CU-Q_2oL questionnaire. In addition, we found a high overall positive correlation ($r = 0.8$) between the CU-Q_2oL and DLQI questionnaire, measures suggesting that they are assessing quite similar content. However, CU-Q_2oL had a better correlation with disease severity, suggest-

ing this should be the preferred questionnaire in future studies. Similar to the German study, quality of life was found to be more severely affected among women than among men; they suffered more from itching, swelling and from embarrassment. General aspects such as sleep problems, difficulty concentrating, eating behavior and medication side effects affected men and women similarly. Other investigators suggested that women are more disturbed by CU symptoms than men because CU has a different etiology or a more severe pathogenesis in women, leading to a more severe outbreak of symptoms [15]. A second potential explanation is that women's skin and/or mental perception is more sensitive to the irritation of CU symptoms, or that CU manifests itself in different anatomic patterns in men and women thereby affecting more sensitive body parts in women than in men [5]. While a patient's disease severity score is a primary consideration in formulating a treatment plan, the CU-Q_2oL scale must also be assessed and integrated into the prescribed therapeutic regimen, which ranges from second-generation antihistamines to cyclosporine or omalizumab [16].

In conclusion, this study demonstrates that the Israeli CU-Q_2oL questionnaire is suitable for use among Israel urticaria patients in both research and clinical settings.

Correspondence
Dr. A. Kessel
Division of Allergy and Clinical Immunology, Bnai Zion Medical Center, Haifa 31048, Israel
Phone: (972-4) 835-9659, **Fax:** (972-4) 835-9961
email: aharon.kessel@b-zion.org.il

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