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Research Article

Transcultural Adaptation and Validation of the Arabic Version of the Compliance Questionnaire for Rheumatology

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Abstract

Background: To date, the Compliance Questionnaire for Rheumatology (CQR) is the only self-reported adherence measure created for and validated in Chronic Inflammatory Rheumatic Diseases (CIRDs). However, it has not been validated in Arabic.

Aim: To translate, culturally adapt, and validate the CQR in Arabic.

Methods: Cross-sectional study, with a longitudinal component to test reliability, using the WHO guidelines: forward and back-translation, cognitive debriefing, and final validation with CIRDs patients (rheumatoid arthritis, spondyloarthritis, connective tissue disease, and Behcet's disease).

Results: The CQR was translated and back-translated by two independent translators, and a cognitive debriefing was performed with 30 patients. For the final validation, 102 patients were included and found that the questionnaire was easy to complete (average time 4.8 minutes). The CQR was significantly associated with self-reported adherence. Test-retest reliability was high (ICC 0.94 (95% CI 0.85 to 0.98)), internal consistency was acceptable (Cronbach α of 0.704). The mean CQR score was 85.4% and was statistically associated with age.

Implications: The CQR was validated in Arabic and can be a useful tool in future clinical and research settings in the Arab world.

Keywords: Compliance; Adherence; Questionnaire; Rheumatoid Arthritis; Spondyloarthritis; Connective Tissue Diseases; Behcet's Disease

Background

Adherence to therapy is a significant challenge in chronic inflammatory rheumatic diseases (CIRDs). Although the efficacy of Disease-Modifying Anti-Rheumatic drugs (DMARDs) is well established, many factors such as delayed efficacy, unpleasant side effects, and specific health belief models may prompt patients to stop taking them [1,2]. According to the World Health Organization (WHO) report on medication adherence, "increasing the effectiveness of adherence interventions may have a far greater impact on the health of the population than any improvement in specific medical treatments" [3].

Suboptimal adherence can lead to disease progression [4], thus increasing the burden on the healthcare system [5]. The apparent treatment "failure" caused by non-adherence can lead to unnecessary treatment escalation resulting in increased costs and decreased quality of life [6].

Medication non-adherence in various chronic illnesses, including CIRDs, is typically estimated to be around 30 to 50% [7-10]. Although physicians tend to agree that adherence is essential, most of them do not systematically measure it during their clinical practice [11]. Moreover, they tend to overestimate it and therefore, they need to use objective assessment tools [12,13].

Many ways of evaluating adherence exist, including direct and indirect measures. Direct measurement of ingestion involves quantifying the concentrations of substances in body fluids. A typical example is dosing serum hydroxychloroquine levels, which correlate with disease activity in systemic lupus erythematosus (SLE) [14]. Biologic assays may seem like the most precise method, but they are not readily available for many drugs; they are expensive and impractical for patients, and their interpretation can be hindered by individual pharmacokinetics. Other direct measurements include direct observation, performed by administering the medication or observing the patient ingesting or auto-administrating it. This method is only practical for single-dose therapies, spaced intermittent administration, or for patients attending infusion centers or hospitals [15]. As for indirect measurements, they are more frequently used and include monitoring pharmacy refills, table counts, the use of electronic devices, and questionnaires [11,12]. Using a validated adherence questionnaire has several advantages over the other methods. It can be done easily without requiring an invasive procedure, is inexpensive, provides relatively accurate measures of true adherence, and can encourage real-life adherence.

To date, the Compliance Questionnaire for Rheumatology (CQR) is the only self-reported adherence measure explicitly created for and validated in rheumatic diseases. It was developed in 1999 in English for patients with rheumatoid arthritis (RA), polymyalgia rheumatica, and gout. This 19-item instrument has encouraging psychometric properties: good test-retest reliability and moderate internal consistency, as per its initial validation using discriminant analyses against an overall patient self-report adherence measure [18]. It was later validated against utilizing electronic medication event monitors (eMEMs), which are currently the gold standard [19]. A shorter version of 5 questions using factor analysis was developed to increase the clinical utility of the questionnaire [20].

In comparison with the Morisky Medication Adherence Scale (MMAS-4), a known generic tool, the CQR appeared to be more sensitive at high levels of adherence [21]. The CQR was validated in French [22], Korean [23], Spanish [24], Italian [25], Turkish [26] and Indian [27] languages.

According to our knowledge, the CQR was never translated or used in Arabic. The Arab world consists of 22 countries in the Middle East and North Africa. Itt includes over 400 million people having a rich diversity of ethnic, linguistic, and religious communities. However, this population shares the same written Arabic language and many cultural similarities [28].

Objectives of the Study

1. The primary objective of our study was to translate, culturally adapt and validate the CQR in Arabic (a-CQR).
2. The secondary objectives were to estimate the mean a-CQR score in patients with CIRDs and to identify the factors associated with this score.

Methods

Study design

The study is cross-sectional, with a longitudinal component for test-retest reliability.

We followed the WHO guidelines for the process of translation and adaptation of instruments [29], which consist of four steps:

1. Forward translation, from English to Arabic, by two independent translators (one informed and one uninformed) and synthesis of the translation by an expert panel (two bilingual rheumatologists, one family physician, and one rheumatology nurse).
2. Back-translation, from Arabic to English, and validation by the expert panel of the first Arabic version a-CQR1.0.
3. Field testing and cognitive debriefing by a trained research nurse on a sample of thirty consecutive CIRDs patients, yielding in the a-CQR1.1 version.
4. Final version validation of the a-CQR1.1 with consecutive patients with CIRDs.

Study population

We included consecutive adult patients with CIRDs (RA, spondyloarthritis (SpA), connective tissue diseases (CTD), and Behcet's disease (BD)) as diagnosed by the rheumatologist, during a routine rheumatology consultation, at two rheumatology clinics. The patients had to be on DMARDs for more than three months and willing to participate in the study. Patients with multiple associated CIRDs

were excluded. All patients signed an informed consent form before completing the questionnaire.

Study procedures

Data were collected over three months using a predefined case report form, including demographics, disease characteristics, current disease activity, comorbidities, and concomitant medication. The translated questionnaire (a-CQR1.0) was self-administered, and then the cognitive debriefing interview was conducted by a trained research nurse.

Cognitive debriefing [30] aims to determine if the target population understands the questionnaire in the translated form the same as the original would be understood. Through a face-to-face interview, the nurse asked the patients to restate in their own words what they thought each translated question means. Complicated and confusing questions were identified at this stage, and errors in understanding were recorded for each patient.

Finally, the validation of the final version (a-CQR1.1) and testing of the psychometric properties were performed using a larger sample of patients. The feasibility was determined by the ability and the easiness of completing the questionnaire. The time needed to complete the questionnaire was recorded. The patients were asked to rate their self-estimation of adherence to chronic treatment on a 4-point Likert scale, ranging from very adherent to non-adherent. The validity of the a-CQR1.1 was tested against this self-reported adherence using one-way ANOVA. The test-retest reliability was evaluated at a one-week interval using the intraclass correlation coefficients (ICCs), by repeating the same questionnaire by the study nurse through telephone contact. The internal consistency was assessed using Cronbach α.

The score calculation was as follows: each item of the CQR was graded from 1 (don't agree at all) to 4 (agree very much), except for questions 4, 8, 9, 11, 12, and 19, which were graded inversely. The CQR-19 is the sum of all the grades minus 19, divided by 0.57 (final percentage of adherence). The total score varies from zero to 100, with a higher score indicating a higher adherence. The CQR-5 is based on questions 2, 3, 5, 6, and 17.

The mean a-CQR1.1 score was calculated and compared between the diseases using one-way ANOVA. A score > = 80% was considered satisfactory, as per previous definitions [19,31-33].

The correlation of the final a-CQR1.1 score with the demographic and clinical data was performed using multiple linear regression. The correlation between a-CQR-19 and a-CQR-5 was performed using the Spearman coefficient.

Statistical considerations

Considering an adherence of 75%, a type I error of 0.05 and a type II error of 0.10, the number needed to include is 38 patients (MedCalc software). We aimed to include around one hundred patients to be consistent with previously published adherence studies and to obtain a balance between the four included diseases. A p-value ≤ 0.05 was considered significant. All other statistical analyses were performed using SPSS V25.0.

Results

Of the 107 consecutive CIRDs patients invited to complete the questionnaire, 102 accepted to participate and were included in the analysis (Patients characteristics in table 1). The five patients who declined stated that they didn't have time to participate. The mean age was 56.3 years (SD 15.1), 75.5% were female, and 44.1% had done university studies. The mean disease duration was 8.7 years (SD 8.3). There were 44.1% of patients with RA, 26.5% with SpA, 23.5% with CTD, and 5.9% with BD.

Population characteristics	**Results**
N	102
Disease, n (%)	
• Rheumatoid Arthritis	45 (44.1%)
• Spondyloarthritis	27 (26.5%)
• Connective Tissue Disease	24 (23.5%)
• Behcet's disease	6 (5.9%)
Mean age in years (SD)	56.3 (15.1)
Female gender, N (%)	77 (75.5%)
Married, N (%)	82 (80.4%)
University studies, N (%)	45 (44.1%)
Employed, N (%)	52 (51%)
Disease duration, years (SD)	8.7 (8.3)
Time since diagnosis, years (SD)	5.3 (6.2)
On conventional DMARDs, N (%)	89 (87.3%)
On biologic DMARDs, N (%)	34 (33.3%)
On targeted synthetic DMARDs, N (%)	11 (10.8%)
DAS-28 in RA, mean (SD)	3.21 (1.3)
Selected Known Comorbidities, N (%)	
• Smoking	32 (31.4%)
• Hypertension	48 (47.1%)
• Dyslipidemia	30 (29.4%)
• Diabetes	14 (13.7%)
• Cancer	4 (3.9%)
• Depression	26 (25.5%)
• COPD/Asthma	5 (4.9%)
• Osteoporosis	26 (25.5%)
Weekly total number of pills, mean (SD)	40.7 (24.8)

Table 1: Population characteristics.

Qualitative evaluation

Phase 1 and 2: Forward and back-translation

The expert panel identified translation discordance in the wording of two questions at this step (Questions 4 and 11 in table 2). The discussion between the expert panel and the translators reached a final agreement on the wording, yielding in the first a-CQR1.0 version.

Phase 3: Field testing and cognitive debriefing

Thirty consecutive patients were included in phase three, and identified the following questions as confusing (Table 2):

Table 2: CQR-19 in the original English version and the translated Arabic versions.

*Questions that were found confusing.

The questions from the first version a-CQR1.0 are in grey; the final version a-CQR1.1 is in black.

- Question 4: The phrase "alternative therapies" was poorly understood as the patient would take an alternative treatment in case the rheumatologist prescribed it.
- Question 8: Was interpreted as a preference for not being sick and, therefore, not having to take any medication.
- Questions 9 and 19 were identified as redundant: This may be because, in our culture, long vacations are not a frequent custom, except for students.
- Question 10: The answer was evidently "yes" since the questionnaire was completed at the rheumatologist's clinic.
- Question 11: The term "miracle" was understood in a religious way of speaking, and it was evident that no miracle could be expected from a simple drug, as miracles are only "the act of God".
- Question 16: Many patients didn't know what the pill organizer was since they were not familiar with this tool in our region.

At the end of this phase, questions 4, 11, and 16 were rephrased. The new version, aCQR1.1, was used for the final validation step by the patients.

Quantitative evaluation: validation of the a-CQR1.1 (phase 4)

All the patients (102) participated in the phase:

- **Feasibility:** The average time to complete the questionnaire was 4 minutes and 48 seconds (SD 41 seconds). The majority of the patients (98%) stated that the questionnaire was easy to complete.
- **Validity:** Using their subjective opinion, most of the patients considered themselves as adherent to therapy (88.2%). The most commonly reported reasons for poor adherence were forgetfulness (20.6%), uncertainty about treatment efficacy (17.6%), treatment cost (15.7%) and fear of side effects (6.9%).

  The validity was estimated in comparison to self-reported adherence. The a-CQR1.1 was significantly lower in the poor adherence group ($p = 0.014$).
- **Reliability:** The test-retest reliability of the a-CQR1.1 was performed at a one-week interval. Agreement between the a-CQR1.1 at time zero and week one was high (ICC = 0.94; range 0.85 to 0.98, $p < 0.001$).
- **Internal consistency:** The internal consistency of the a-CQR1.1 was calculated, yielding a Cronbach α of 0.704, which is in the acceptable range.
- **Score calculation:** The mean a-CQR v1.1 score was 85.4% (SD 8.2), ranging from 52% to 100%. Seventy-eight percent of the patients had a satisfactory score (as defined by a threshold of > = 80%). In bivariate analysis, the a-CQR1.1 correlated with age (higher in older patients, $p = 0.007$), gender (higher in females, $p = 0.035$), disease (higher in RA, $p = 0.042$), total number of comorbidities ($p = 0.005$), but not with individual comorbidities. On the other hand, it was not correlated with the total number of pills per week, educational level, disease activity, and disease duration. In multivariable analysis, only age remained statistically associated with the a-CQR1.1 score ($p = 0.001$).

The mean a-CQR-5 score was 98.7% (SD 3.8), ranging from 85% to 100%. The correlation between a-CQR-19 and a-CQR-5 was statistically significant ($p = 0.024$) but considered low with a Spearman coefficient of 0.369 (lower than the 0.7 acceptable threshold).

Discussion

We translated, culturally adapted, and validated the Arabic version of the CQR (a-CQR1.1), using the WHO methodology, to provide a useful tool in estimating adherence in the Arab countries. Three questions were rephrased to be better understood in the cultural setting. As in the Korean version [23], question 16 about the pill organizer was rephrased as this tool is not widely used in our region.

The a-CQR1.1 was well accepted among CIRDs patients, quick and easy to perform. The time required to complete was relatively short, even shorter than the timing described in the previous international versions. The a-CQR was shown valid compared to self-reported adherence. The test-retest reliability at one week was high (0.94), higher than the English (0.73) [18], Spanish (0.76) [34] and Korean versions (0.71) [23], which were tested at two-weeks intervals. The internal consistency was acceptable, slightly lower than the Spanish version [34].

Our population showed a high mean level of adherence (a-CQR1.1 = 85.4% (SD 8.2)), as defined by the 80% cut-off [18,31-

33]. The mean a-CQR1.1 was slightly higher than the one observed in the English (76.6% (SD 12.8)) [32], French (75%) [22], Korean (61.4% (SD 5.97)) [23] and Turkish versions (69.2%) [26], but was in the same range of the Spanish (79.1%) [31] and the Indian versions (86.4%) [27].

Based on the work of de Klerk., *et al*. who found that the sensitivity of CQR to detect adherence = < 80% was 62% [32], we could have an estimation of the real meaning of the CQR in a research setting. For example, we could roughly estimate that a CQR score of 85.4% reflects a true adherence around 53%, which corresponds to the published data on adherence in chronic diseases [7-10].

Subjective adherence was also clearly overestimated in our study, with most of the patients subjectively considering themselves as totally or moderately adherent to therapy (97.1%). This result confirms that this subjective assessment is poorly useful for the realistic estimation of adherence [12,13].

A potential explanation of this high level of reported adherence may be due to answering the questionnaire at the rheumatology clinic, which may influence the patient's responses [12,13]. However, the questionnaire was completed in a separate office. It was not viewed by the rheumatologist at the time of completion, to reduce any doctor's influence.

Self-reported poor adherence was related mainly to forgetfulness (unintentional non-adherence), uncertainty about treatment efficacy (patients' concerns and belief models), and treatment cost, as in the identified factors by WHO [3]. Interestingly in our study, fear of side effects was not a major obstacle to adherence.

The a-CQR1.1 score was higher in RA patients in bivariate analysis. This issue is controverted across studies, with some reports that suggested lower adherence in SLE compared to RA, whereas others found no differences [32,35-38].

In our study, a higher a-CQR1.1 was associated with age, similarly to the literature, with older patients having higher adherence scores [31,39,40]. This finding could be explained by the wisdom that patients may acquire with age, which makes them more adherent to the physician's recommendations. We identified some factors associated with a-CQR1.1 in the bivariate analysis only, reflecting the literature: female gender, the number of comorbidities [31,40]. We didn't find any association with the class of medication as in other studies [19]. However, the low sample size of our study may have prevented reaching statistical significance.

Many studies found an association between adherence and the relationship with the medical team, the confidence in the rheumatologist, and the medication necessity beliefs [31,40-45]. Although not formally identified by our study, these factors were partially reflected in the "uncertainty about treatment efficacy" stated by our patients as a reason for poor adherence.

Due to the low correlation found between the full version (CQR-19) and the short version (CQR-5), with the latter seeming less discriminating and potentially less sensitive to change, the expert panel decided to recommend the full version for the future use. The time to complete the questionnaire in its full version was acceptable, especially that it is used as an auto-questionnaire, which does not take any time from the clinical consultation.

The main limitation of our study is its low sample size. However, our sample size remains consistent with previous validation studies (median number in studies was 41 to 274 patients) [22-26,46]. Also, we didn't test the construct validity of the questionnaire against pharmacy refills or electronic devices as this is not the objective of our study, as we consider that CQR validity is already established. Moreover, drug dispensing in our country is liberal and almost impossible to track with precision.

The CQR may have some disadvantages: it is an indirect measure, the patients may refuse to complete it or over-report their level of adherence. However, despite its limitations, the CQR has many advantages over other adherence-measuring methods. It is simple, quick, acceptable, easy to read and to understand by the patients, and can be administered easily without the help of an investigator. It can also identify areas of poor adherence specific to one patient and improve patient adherence to treatment. Additionally, it may screen poorly adherent patients before inclusion in a clinical trial or, at the individual level, before starting a specific drug. Finally, in the current study, a-CQR1.1 was validated in a representative sample of several CIRDs with a good range of diseases' types and duration.

Conclusion

CQR-19 was translated, culturally adapted, and validated in Arabic. It showed to be relatively easy to perform by CIRDs patients

and had a good reliability and an acceptable internal consistency. Therefore, the a-CQR1.1 could be considered as a useful tool in future clinical and research settings in the Arab world.

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