Original Article

Validity, Reliability and Factor Structure of Hepatitis B Quality of Life Questionnaire Version 1.0: Findings in a Large Sample of 320 patients

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Abstract

Background: Quality of life is of significant importance in chronic hepatitis B (CHBV). We aimed to assess the psychometric properties of the Hepatitis B Quality of Life Questionnaire v1.0 (HBQOL) in a large sample of 320 Iranian patients with CHBV.

Methods: After adapting the Iranian version through forward-backward translation and expert panel discussion, we administered HBQOL together with Short-Form 36 (SF-36), Medical Outcome Study Social Support Questionnaire (MOS-SS), Hospital Anxiety and Depression Scale (HADS), and the Iowa Fatigue Scale (IFS) to 320 non-cirrhotic Iranian patients. We used principal component analysis with Varimax rotation to determine the factor structure. To evaluate the psychometric properties of HBQOL, test-retest and internal consistency reliabilities, divergent and convergent validity with other instruments, and discriminatory power were calculated.

Results: Thirty-one questions loaded on to six factors (Anticipation anxiety, Stigma, Psychological well-being, Vitality, Transmissibility and Vulnerability) which explained 63.6% of total variance. Test-retest reliability was 0.66. Cronbach's α was 0.94 for the overall scale and between 0.7 and 0.9 for subscales, with the exception of the Vulnerability subscale. HBQOL and its subscales showed acceptable convergent and divergent validity with other instruments. Furthermore, Vulnerability subscale of HBQOL discriminated between patients with chronic active and chronic inactive hepatitis.

Conclusion: The Iranian version of HBQOL is reliable, valid, and sensitive to the clinical conditions of the patients. This instrument has acceptable factor structure to measure several aspects of quality of life in patients with chronic HBV.

Keywords: Anxiety, depression, factor analysis, fatigue, hepatitis B quality of life questionnaire version 1.0, reliability, validity

Introduction

I n recent years, health-related quality of life (HRQOL) has become a main measure of health and an important outcome in clinical trials. Although clinicians are more concerned with the biological outcomes of their patients, patients mainly worry about their quality of life.[1] Chronic diseases can negatively affect HRQOL and chronic hepatitis B (CHBV) is no exception. Several studies have shown impairment of HRQOL in patients with CHBV.[2–6] Instruments to assess HRQOL consist of two different categories: generic and disease-specific. Generic instruments can be used for all disease types and allow for comparison among diseases, whereas disease-specific instruments focus on a specific disease or a specific group of diseases, evaluating the condition in a more specific manner.[1] Two of the most important features of disease-specific questionnaires which make them useful outcome measure, particularly in clinical trials, are their capability to differentiate between different severities of the disease as well as their sensitivity to change in clinical condition over time.[7]

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Because biological outcomes or generic instruments may miss key disease-related components of HRQOL and overlook patients' perceptions of their HRQOL, a disease-specific instrument seems necessary.[7] Until 2007, the measures used for evaluation of HRQOL in patients with CHBV were either generic [i.e., Short Form-36 (SF-36)] or liver-specific (but not CHBV-specific) quality of life questionnaires such as the Chronic Liver Disease Quality of Life Questionnaire (CLDQ) and the Liver Disease Quality of Life Questionnaire (LDQLQ).[8–10]

In 2007, Spiegel et al.[11] developed a disease-targeted quality of life questionnaire for non-cirrhotic patients with CHBV entitled the Hepatitis B Quality Of Life Instrument, version 1.0 (HBQOL v1.0). Their factor analysis showed the following six distinct factors: Psychological well-being, Anticipation anxiety, Vitality, Stigma, Vulnerability, and Transmissibility. An extra *a priori*-defined factor, related to Viral response, was also added which was a combination of Vulnerability and Transmissibility. They described high test-retest reliability, internal consistency, and discriminant validity for the questionnaire. However, after development of the HBQOL, no study evaluated the psychometric characteristics of the questionnaire. Additionally, this instrument has not been evaluated in different cultural contexts. CHBV is quite prevalent in Asian countries and the results from the English version cannot be generalized to other languages and cultures.

To assess the psychometric properties of HBQOL in a larger sample of non-cirrhotic patients with CHBV and to evaluate the questionnaire in people with different cultural and language back-

Table 1. Instruments used in the validation of HBQOL.

Instrument	Developers/year [reference number]	Number of items	Subscales	Cronbach's α	Adapting the Iranian version [Reference number]	Cronbach's α of the Iranian version
Short-Form 36	Ware and Sherbourne/ 1992[13]	36	Mental and physical component summary (MCS and PCS)	> 0.85	Montazeri et al.[14]	0.65– 0.9
Medical Outcome Study Social Support Questionnaire	Sherbourne and Stewart /1991[13]	19	Emotional/Informational support, Tangible support, Affection, Positive interaction	> 0.9	Our group	0.95
Iowa Fatigue Scale	Hartze el al./ 2003[15]	11	Cognitive, Fatigue, Energy, Productivity	0.9	Our group	0.81
Hospital Anxiety and Depression Scale	Zigmond and Snaith/ 1983[16]	14	Anxiety, Depression	Anxiety: 0.8 Depression: 0.76	Montazeri et al.[17]	Anxiety: 0.78 Depression: 0.86

grounds, we administered HBQOL to Iranian patients with CHBV. Next, we performed a factor analysis and determined the questionnaire's reliability. To ensure the convergent and divergent validity of HBQOL, we used several generic instruments.

Materials and Methods

Subjects

From March to September 2010, we evaluated 320 patients with CHBV who referred to a university clinic in Shariati Hospital, Tehran, Iran. Inclusion criteria were: confirmed CHBV diagnosis, age > 18 years, and ability to communicate. Co-infection with hepatitis C or HIV, severe psychiatric disorders and any other severe comorbid diseases were exclusion criteria. All patients read and signed an informed consent form. The Ethics Committee of the Digestive Disease Research Institute of Shariati Hospital approved the proposal.

Data collection

Two trained interviewers collected important baseline characteristics and clinical data in separate questionnaires. In addition to HBQOL, we administered several generic questionnaires to evaluate quality of life, social support, fatigue, depression, and anxiety with the intent to determine the convergent and divergent validity of HBQOL. Because of the large number of questions, we administered each instrument to a proportion of patients, so that each patient completed two or three questionnaires in addition to the HBQOL. All questionnaires were self-administered and interviewers were responsible for interviewing illiterate patients as well as supervising other patients as they completed the questionnaires.

Assessment instruments

HBQOL[11] consists of 31 questions. Each contains a 5-point Likert-type scale and is loaded onto six factors: Psychological well-being, Anticipation anxiety, Vitality, Stigma, Vulnerability, Transmission (plus *a priori* defined factor, Viral response). Cronbach's α was 0.96 for the overall score and with a range of 0.75 – 0.9 for subscales. The scale showed high test-retest reliability and its related subscales showed high convergent validity with SF-36 MCS and PCS (mental and physical component summaries). Spiegel et al.[11] found high discriminatory power of the viral response item between viral responders and viral non-responders.

Similar to the study by Spiegel et al.[11] ,we changed the total score of HBQOL (range: 31 – 155) to a 100-point scale with lower scores showing lower quality of life. We used forward-backward

translation recommended by World Health Organization to adapt the Persian version of the HBQOL.[12]

We used the following four generic questionnaires: i) SF-36,[13,14] ii) Iowa Fatigue Scale (IFS),[15] Medical Outcome Study Social Support Questionnaire (MOS-SS),[13] and the Hospital Anxiety and Depression Rating Scale (HADS).[16,17] Table 1 provides a summary of these instruments.

There are several "rules of thumb" for determining sample size in factor analysis. Many authors believe that a sample size of 10 individuals per item, 50 individual per factor, or at least 300 is adequate.[18] For the purpose of this study, we determined a sample size of 300, with an additional 20 subjects for possible missing data. Since the completed questionnaires were examined for completeness by the interviewer before the patient left the clinic, we considered a 7% loss of samples rather than the more routine 15%.

The first 300 patients also completed other questionnaires based on a random block method. There were 13 blocks, each of which contained 23 individuals who were given the questionnaire. Based on another "rule of thumb" for bivariate correlation, a sample size of more than 100 (according to some, 104) is considered appropriate. However some authors consider numbers as low as 50 to be acceptable.[18,19] Thus, we have applied a ratio of 1.875 (15/8 in each block) and the overall MOS-SS was administered to 104 patients. The other patients received HADS and IFS questionnaires. Since SF-36 was the main measure of validity in our study, it was administered to as many patients as possible, unless time limitations of the clinic prevented us from doing so.

Data analysis

SPSS version 15.00 (Chicago, USA) was used for data analysis. We used exploratory factor analysis (principal component analysis) with Varimax rotation with Kaiser Normalization.[20] Factors with eigenvalues of more than one were retained for analysis. Items, which loaded more than 0.4 onto at least one factor and ranked first or second in the scale loadings, were retained in that factor. In addition, we determined the inclusion or exclusion of an item in a factor based on face validity (i.e., discussion with our expert panel). To evaluate the quality of sampling, we used Kaiser-Meyer-Olkin (KMO) and Bartlett's test of sphericity.

To report the score of our patients, we used the 100-point scale with higher scores showing better quality of life. Skewness was used to evaluate data distribution. To compare subgroups, the parametric tests was used for normally distributed data whereas the non-parametric tests were used for skewed data. Floor and ceiling effects were noted to be present if 15% of participants achieved the

lowest or highest possible scores.[21]

To calculate test-retest reliability, we administered the HBQOL to a number of patients two weeks after the first administration and calculated the intraclass correlation coefficient.[22] To determine the internal consistency we calculated Cronbach's α for each factor and for the overall HBQOL score. Cronbach's α of 0.7 or more was considered acceptable.

To determine questionnaire validity, we assessed content validity, construct validity, and discriminatory power of the questionnaire.[23–25] Developers of the questionnaire had approved the content validity in their own study. Besides, we discussed the translated questionnaire with a number of experts in the fields of hepatology, psychology, and psychometrics to ensure its content validity.

Construct validity determines how much a questionnaire measures the construct of interest. To determine construct validity, we evaluated both convergent and divergent validities.[23] There are many ways to assess these validities; all equally efficient. What is consistent among all studies for assessment of construct validity is correlational analysis.

Convergent validity is the correlation of the questionnaire with other well-validated instruments that have the same construct (i.e., measuring the same thing). A correlation coefficient of 0.21 to 0.4 is considered fair, 0.41 to 0.6 is good, 0.61 to 0.8 is very good, and more than 0.8 is excellent.[26] A good correlation coefficient was considered evidence of good convergent validity in our study. We hypothesized that MCS, depression, and anxiety should have at least good correlation with the mental-related subscales of HBQOL (most importantly Psychological well-being, and Anticipation anxiety), while PCS and IFS should have at least good correlation with the physical-related subscales of HBQOL (Vitality). In addition, these factors should be less correlated with other less-related subscales when compared with their correlation with more-related subscales.

Divergent validity shows how much an instrument correlates with a construct that it should not measure.[23,25] We determined divergent validity by calculating the correlation of HBQOL and MOS-SS, each of which were designed to measure completely different constructs. Therefore, we hypothesized that HBQOL, although related to social support should have a fair correlation (0.2 – 0.4) with MOS-SS.

The discriminatory power of an instrument shows the ability of an instrument to discriminate between two clinically distinct conditions. Any outcome measure intended for health care purposes should be sensitive to changes in health status. In the study by Spiegel et al., this was determined as the capability of the Viral response subscale to distinguish between viral responders and nonresponders. Since the design of the present study was not longitudinal, we determined discriminatory power by a comparison of HBQOL and its subscale scores between patients with chronic active hepatitis (CAH) and patients with chronic inactive hepatitis (CIH).

Results

Sample characteristics and HBQOL scores

A total of 320 patients (110 females and 210 males) with a mean ± SD age of 39.6 ± 13.4 years participated in the study. No significant difference was observed in age, gender, marital status or educational level between patients who were administered a particular questionnaire and those who were not given that question-

naire. Table 2 shows baseline characteristics of participants. Because of supervision at the time of administration of the questionnaires, none of the questionnaires had missing data. Mean time for completion of HBQOL was 6 (3 to 10) minutes. The overall score and scores of factors one to four on the percentile scale had a negative skewed distribution (better quality of life) while factors five to seven showed normal distribution. The mean ± SD score for HBQOL was 66.12 ± 20.90. Patients with recently diagnosed CHBV showed lower scores of HBQOL and its subscales (except Vulnerability) than the patients with previously diagnosed CHBV ($P < 0.05$ for Vitality, and $P < 0.01$ for overall scale and other subscales). Of patients, 0.9% achieved the highest possible score, whereas 0.9% also achieved the lowest possible scores which indicated the absence of floor and ceiling effects. The effects of several variables on scores of the HBQOL scale and its subscales are shown in Table 3.

Table 2. Baseline characteristics of patients.

Variable	Value
Male gender (%)	210 (65.6%)
Age (mean ± SD)	39.63 ± 13.37
Educational level	
Illiterate (%)	43 (13.5%)
Less than diploma (%)	120 (37.5%)
Diploma (%)	96 (30%)
BS (%)	51 (15.9%)
MS and over (%)	10 (3.1%)
Residence	
Capital (%)	127 (39.7%)
Other cities (%)	193 (60.3%)
Marital status	
Single (%)	50 (15.6%)
Married (%)	263 (82.2%)
Divorced (%)	7 (2.2%)
Widowed (%)	0 (0%)
Habitual history	
None (%)	226 (70.6%)
Cigarette (%)	67 (20.9%)
Alcohol (%)	50 (15.6%)
Illicit drug (%)	24 (7.5%)
Comorbid conditions (%)	85 (26.5%)
Possible transmission route	
Vertical (%)	68 (21.25%)
Sex (%)	2 (0.6%)
Blood-born (%)	32 (10%)
Unknown (%)	218 (68.15%)
Chronic active hepatitis (%)	72 (22.5%)
Time since diagnosis (mean ± SD)	68.1 ± 68.6 (month)
Recently (< 6 months) diagnosed patients (%)	59 (18.4%)
SF-36 scores	
PCS (mean ± SD)	47.9 ± 9.1
MCS (mean ± SD)	47.2 ± 11.5
HADS scores	
Anxiety (mean±SD)	7.5±4.6
Depression (mean±SD)	4.6±4.1
IFS score (mean±SD)	26.8±8.3
MOS-SS score (mean±SD)	73.6±17.7

Factor analysis

A six-factor solution emerged accounting for 63.6% of the total variance. The KMO test was 0.938 and Bartlett's test of sphericity was significant at a level of $P < 0.001$, which showed high quality of the sampling. Anticipation anxiety, with eight items, explained 15.5% of the variance followed by Stigma, Psychological well-being, Vitality, Transmissibility, and Vulnerability. We also included the Viral response factor, which consists of items of Transmissibility and Vulnerability (Table 4). After primary analysis, because Productivity (F12) loaded onto the Psychological well-being (it loaded onto Vitality in the study by spiegel et al.) we hypothesized

Table 3. Effect of several variables on HBQOL and its subscales.

Variable	HBQOL components							
	Anticipation anxiety	Stigma	Psychological well-being	Vitality	Transmissibility	Vulnerability	Viral response	HBQOL
Gender								
Female	57.5 ± 27.4	76.7 ± 24.3	68.8 ± 24.6	63.3 ± 27.9	56.8 ± 35.7	48.4 ± 30.9	52.6 ± 24.6	64.9 ± 20.9
Male	62.7 ± 26.0	73.7 ± 24.5	71.7 ± 24.8	68.5 ± 26.7	52.6 ± 37.1	48.8 ± 30.2	50.7 ± 26.3	66.7 ± 20.9
Age	r = 0.062	r = 0.078	r = 0.100	r = 0.025	r = -0.030	r = 0.006	r = -0.013	r = 0.062
Duration	r = -0.069	r = 0.024	r = 0.072	r = -0.060	r = 0.057	r = -0.027	r = 0.043	r = 0.008
Diagnosis								
Recent	52.5 ± 28.0**	67.7± 24.0**	56.8 ± 25.0**	58.7 ± 29.7*	41.5 ± 37.0**	43.2 ± 31.3	42.3 ± 26.5**	56.6 ± 20.1**
Past	62.8 ± 25.9	76.4 ± 24.2	73.8 ± 23.6	68.5 ± 26.3	56.9 ± 36.0	49.9 ± 30.2	53.4 ± 25.1	68.2 ± 20.5
Living in								
Tehran	62.1 ± 28.0	75.4 ± 23.9	71.9 ± 25.2	66.4 ± 27.8	59.3 ± 36.0*	48.6 ± 30.2	53.9 ± 24.9	67.1 ± 21.4
Other cities	60.2 ± 25.6	74.3 ± 24.8	69.9 ± 24.5	66.9 ± 26.9	50.6 ± 36.8	48.7 ± 30.7	49.7 ± 26.2	65.4 ± 20.5
¹Marital status								
Single	63.3 ± 26.0	72.0 ± 24.8	67.5 ± 26.5	68.1 ± 30.7*	60.0 ± 35.1	47.7 ± 24.5	53.8 ± 23.0	65.7 ± 65.7
Married	60.4 ± 26.6	75.1 ± 24.4	71.2 ± 24.3	67.2 ± 26.2	52.4 ± 36.9	49.1 ± 29.7	50.7 ± 26.3	66.1 ± 66.1
Divorced	61.1 ± 32.3	82.6 ± 25.9	73.2 ± 29.5	39.2 ± 25.1	75.0 ± 32.2	39.2 ± 27.4	57.1 ± 20.8	65.7 ± 65.7
Educational level								
Less than diploma	61.7 ± 27.6	72.4 ± 26.1	68.8 ± 26.8	64.5 ± 28.3*	54.2 ± 36.8	47.8 ± 29.3	51.0 ± 24.4	64.9 ± 21.9
Diploma and over	61.8 ± 25.9	77.0 ± 23.3	73.5 ± 22.9	72.4 ± 25.2	56.7 ± 36.7	51.2 ± 31.9	54.0 ± 26.9	68.6 ± 20.2
Comorbid disease								
No	62.5 ± 26.1	74.4 ± 25.4	72.6 ± 24.6	70.8 ± 26.8**	57.3 ± 36.6	50.1 ± 30.9	53.7 ± 25.4	67.7 ± 20.9
Yes	59.5 ± 28.7	75.1 ± 23.6	66.8 ± 26.2	61.3 ± 27.0	50.1 ± 36.7	47.6 ± 30.0	48.9 ± 26.1	63.8 ± 21.5
Viral activity status								
Active	60.7 ± 28.7	75.6 ± 24.6	71.4 ± 22.5	65.4 ± 27.2	56.9 ± 37.6	37.8 ± 27.4**	47.3 ± 25.6*	65.7 ± 19.8
Inactive	61.0 ± 26.0	74.5 ± 24.5	70.5 ± 25.4	67.1 ± 27.2	53.2 ± 36.4	51.8 ± 30.6	52.5 ± 25.7	66.2 ± 21.2

Values are presented as mean ± SD. * = $P < 0.05$; ** = $P < 0.01$; r = Spearman ranked correlation coefficient; ¹Vitality scores differ between married and divorced, single and divorced patients.

that patients may have different concepts of Productivity based on educational level. We found that in patients with lower educational levels, Productivity loaded more onto Vitality than other factors.

Reliability, validity, and discriminatory power

Testing of internal consistency showed satisfactory Cronbach's α for five of the six main subscales (Anticipation anxiety = 0.9, Stigma = 0.86, Psychological well-being = 0.88, Vitality = 0.83, Transmissibility = 0.7, Vulnerability and Viral response = 0.55). HBQOL total scores had Cronbach's α of 0.94. The Vulnerability subscale had a Cronbach's α of < 0.6 which showed poor, but not 'unacceptable' coefficient.[7] Substantial (defined as > 0.6) test-retest reliability was observed in 29 patients who were retested two weeks after the initial questionnaire administration (ICC = 0.660).

Scores of MCS and PCS significantly correlated with HBQOL scores. However, the strength of correlation was higher for MCS (r = 0.616 for MCS and 0.399 for PCS; $P < 0.001$). In addition, among the subscales, the Psychological well-being factor had the highest correlation with MCS (r = 0.646, $P < 0.001$). Among the HBQOL subscales, Vitality had the highest correlation with both PCS and IFS (Table 5). As seen in Table 5, Anxiety had the strongest relation with Psychological well-being (r = -0.625, $P < 0.001$) while depression had the highest correlation with Vitality (r = -0.621, $P < 0.001$). There was a significant correlation between HBQOL and MOS-SS scores (r = 0.322, $P < 0.001$). Of the HBQOL subscales, the strongest relation was between Vitality and MOS-SS (r = 0.422, $P < 0.001$) followed by Psychological well-

being and MOS-SS (Table 5).

Vulnerability and Viral response discriminated between patients with CAH and patients with CIH (defined by viral load and liver enzymes) and thus showed discriminatory power ($P < 0.001$ for Vulnerability and $P < 0.05$ for Viral response).

Discussion

The present study was the first, to our knowledge, which evaluated HBQOL after its development. Two of the main advantages of our study were its large sample size and the use of several instruments to validate HBQOL. Our results showed that the Vulnerability subscale was able to differentiate between patients with CAH and CIH. According to Spiegel et al.[11] the Viral response factor discriminated between viral responders and non-responders. While we found that the same factor was able to distinguish between patients with CAH and CIH, this was totally attributable to the Vulnerability subscale, which was a subset of the Viral response factor. Because the design of the present study was cross-sectional, we were unable to detect any "change" in our patients. The difference between patients with normal and abnormal liver functions has been shown in other studies that used different instruments. Lam et al.[5] and Ong et al.[4] showed that the Worry subscale of the CLDQ and MCS subscale of SF-36 were capable of differentiating between patients with normal and abnormal liver function, respectively.

The recent diagnosis of CHBV significantly affected our patients'

Table 4. Factor structure of HBQOL v1.0.

Items	Components					
	1 (Anticipation anxiety)	2 (Stigma)	3 (Psychological well-being)	4 (Vitality)	5 (Transmissibility)	6 (Vulnerability)
C1: Concern failure	**0.782**	0.141	0.119	0.185	0.023	0.071
C2: Concern cancer	**0.719**	0.280	0.091	0.187	0.187	-0.077
C15: Concern worsen	**0.660**	0.203	0.216	0.126	0.296	0.165
C5: Concern flare	**0.653**	0.236	0.100	0.076	0.404	0.157
C12: Concern survival	**0.622**	0.249	0.204	0.146	0.371	0.131
F9: Bad	**0.608**	0.214	0.468	0.086	0.056	0.015
C6: Concern sick easily	**0.606**	0.133	0.092	0.185	0.306	0.192
C9: Concern survival	**0.504**	0.326	0.322	0.207	0.190	0.170
F2: Stigmatized	0.188	**0.762**	0.072	0.095	-0.075	0.046
F1: Ashamed	0.164	**0.625**	0.334	0.009	0.048	0.074
C14: Concern embarrassed	0.185	**0.603**	0.347	0.076	0.317	0.085
C3: Concern boss	0.247	**0.569**	0.003	0.123	0.183	0.016
F8: Isolated	0.188	**0.565**	0.451	0.138	0.149	0.012
C11: Concern socially isolated	0.186	**0.557**	0.349	0.209	0.414	0.051
C10: Concern self-conscious	0.209	**0.554**	0.446	0.101	0.362	0.088
F4: Frustrated	0.216	0.532	**0.492**	0.224	-0.030	-0.055
F3: Sad	0.408	0.486	**0.422**	0.128	-0.060	-0.017
F10: Less enjoyable	0.203	0.286	**0.684**	0.195	0.108	0.051
F11: Sex difficult	0.033	0.109	**0.680**	0.188	0.153	0.307
F13: Scared	0.559	0.118	**0.632**	0.115	0.024	0.002
F7: Angry	0.207	0.226	**0.575**	0.227	0.075	-0.050
F6: Anxious	0.458	0.259	**0.523**	0.255	-0.027	-0.044
F12: Unproductive	0.022	0.370	**0.523**	0.346	0.242	-0.067
P3: Muscle aches	0.202	-0.003	0.152	**0.796**	0.031	0.075
P1: Tiredness	0.215	0.249	0.212	**0.787**	0.018	0.043
P2: Memory problems	0.125	0.069	0.182	**0.733**	0.128	0.048
F5: Worn out	0.210	0.430	0.302	**0.599**	-0.090	0.089
C4: Concern transmit child	0.208	0.079	0.071	-0.006	**0.759**	-0.027
C7: Concern transmit sex	0.318	0.084	0.087	0.062	**0.730**	0.084
C13: Concern eat	0.026	0.076	0.142	0.001	0.071	**0.800**
C8: Concern medicines	0.239	0.015	-0.070	0.139	-0.001	**0.771**
Rotated eigenvalues	4.8	4.1	4.0	2.8	2.2	1.5
Variance explained (%)	15.5%	13.4%	13.1%	9.2%	7.3%	4.9%

Table 5. Spearman's ranked correlation coefficient (95% CI) between HBQOL and other instruments

Instruments	HBQOL components						
	Anticipation anxiety	Stigma	Psychological well-being	Vitality	Transmissibility	Vulnerability	HBQOL total score
PCS	r = 0.340** (0.209 to 0.458)	r = 0.230** (0.101 to 0.367)	r = 0.402** (0.277 to 0.514)	r = 0.544** (0.437 to 0.636)	r = 0.057 (-0.084 to 0.196)	r = 0.082 (-0.059 to 0.220)	r = 0.399** (0.273 to 0.510)
MCS	r = 0.508** (0.396 to 0.605)	r = 0.506** (0.393 to 0.603)	r = 0.646** (0.556 to 0.721)	r = 0.627** (0.534 to 0.705)	r = 0.179* (0.040 to 0.312)	r = 0.043 (-0.098 to 0.182)	r = 0.616** (0.521 to 0.696)
IFS	r = -0.544** (-0.636 to -0.437)	r = -0.450** (-0.555 to -0.330)	r = -0.608** (-0.689 to -0.511)	r = -0.681** (-0.750 to -0.598)	r = -0.215** (-0.345 to -0.077)	r = -0.099 (-0.237 to 0.042)	r = -0.625** (-0.704 to -0.531)
Anxiety	r = -0.616** (-0.696 to -0.520)	r = -0.511** (-0.608 to -0.400)	r = -0.625** (-0.700 to -0.526)	r = -0.620** (-0.700 to -0.526)	r = -0.202** (-0.333 to -0.063)	r = -0.171* (-0.304 to -0.031)	r = -0.666** (-0.738 to -0.580)
Depression	r = -0.492** (-0.592 to -0.378)	r = -0.435** (-0.542 to -0.314)	r = -0.507** (-0.681 to -0.499)	r = -0.621** (-0.701 to -0.527)	r = -0.190** (-0.322 to -0.051)	r = -0.090 (-0.227 to 0.051)	r = -0.587** (-0.672 to -0.487)
MOS-SS	r = 0.216* (0.024 to 0.392)	r = 0.281** (0.094 to 0.449)	r = 0.366** (0.187 to 0.522)	r = 0.422** (0.249 to 0.568)	r = 0.056 (-0.138 to 0.246)	r = -0.045 (-0.235 to 0.149)	r = 0.322** (0.138 to 0.485)
* = P<0.05; ** = P <0.01.							

HRQOL. Patients who were diagnosed for longer durations might have adopted coping mechanisms which might have lowered the influence of CHBV on their HRQOL.

Although the present study confirms the psychometric properties reported by the primary study, some points need clarification. For example, items F9 and C6 loaded onto Anticipation anxiety in our study (rather than Psychological well-being and Vitality in the original questionnaire). Regarding face validity, both items point out a "future" incident and may be more appropriately considered under Anticipation anxiety.

While Stigma was the fourth important factor in the study by Spiegel et al.[11], it was the second most important factor in our work. This may reflect cultural differences between the populations of these studies, as the rate of perceived stigma in patients

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Table 6. Comparison of HBQOL with other liver disease-related HRQOL questionnaires.

Questionnaire	Developer(year)	Number of questions	Time needed to complete	Subscales	Reliability	Validity
Chronic Liver Disease Questionnaire	Younossi et al.[10] (1999)	29(previous two weeks)	10 min	Fatigue, Emotional function, Worry, Abdominal symptoms, Activity, Systemic symptoms, Sleep (new subscale)	α = 0.72 – 0.95 Test-retest: 0.58 – 0.79	Related subscales: 0.69 – 0.85 Unrelated subscales: 0.33 – 0.48
Hepatitis Quality of Life Questionnaire	Bayliss et al.[32] (1998)	69 (previous four weeks)	NA	All eight SF-36 subscales, Sleep, health distress, CHC distress, CHC limitations	α = 0.81 – 0.94	Related subscale: > 0.6 Unrelated subscale: 0.33
Liver Disease Symptoms Index	Unal et al.[33] (2001)	12 (previous one week)	<6 min	Itching, Joint pain/discomfort, Pain in the upper abdomen, Drowsiness, Sleeping during the day, Lack of appetite, Fear of complications	α = 0 .79 – 0.86 Test-retest: 0.72 – 0.84	Unrelated subscales: < 0.6
Liver Disease Symptoms Index 2.0	Van der Plas et al.[34] (2004)	18 (previous one week)	NA	Itch, Joint pain, Pain in the right upper abdomen , Sleepiness during the day, Worry about family situation, Decreased appetite, Depression, Fear of complications, Jaundice	$\alpha \geq$ 0.79 Test-retest: 0.55 – 0.99	Related subscales: 0.52 – 0.8
Liver Disease Quality of Life Questionnaire	Gralnek et al.[9] (2000)	111 (previous four weeks)	38.3 min	All eight SF-36 subscales, Symptoms of liver disease, Effects of liver disease , Concentration, Memory, Quality of social interaction, Health distress, Sleep , Loneliness , Hopelessness, Stigma of Liver disease , Sexual functioning, Sexual problems	α = 0.62 – 0.95	Worse HRQOL is associated with worse severity
Hepatitis B Quality of Life Questionnaire 1.0	Spiegel et al.[11] (2007)	31	6 min	Psychological wellbeing, Anticipation anxiety, Vitality, Stigma, Transmissibility, Vulnerability, Viral response	α = 0.73 – 0.96 test-retest = 0.96	Related subscales: 0.55 Unrelated subscale < 0.4

α = Cronbach's α; Numbers under Validity column show correlation coefficients. Test-retest values show intra-class correlation coefficients.

with chronic conditions in developing countries is twice as high as developed countries.[28] Furthermore, while item F8 was considered an item of psychological well-being in the primary study, it was related to Stigma in the present work. In a study on HIV patients, Fife and Wright found four distinct dimensions for stigma: social rejection, financial insecurity, internalized shame, and social isolation.[29] Of note, because in HBQOL at least three of these four dimensions (other than financial insecurity) are addressed, this tool may be considered a disease-specific tool for stigma.

Eight items loaded on to Psychological well-being in our study, six of which were common between our study and the study by Spiegel et al.[11] Two items, sexual activity (F11) and productivity (F12), loaded on Psychological well-being, while in the primary study F11 loaded on to Transmissibility and F12 loaded on to Vitality. However, F12 was loaded on Vitality in less educated patients. Vitality mainly consists of items that describe physical function (as shown by its high correlation with PCS and IFS). Because educational level is regarded as a key item in socioeconomic status, it may be interpreted that patients with lower educational levels rely more on their physical function to do their jobs; so they consider their productivity as an important consequence of their physical function, rather than psychological well-being. Surprisingly, the item "I feel like sexual activity is difficult for me because of hepatitis B" loaded mostly on to Psychological well-being, than

Transmissibility. However, in the primary study, the loading of this item differed only 0.05 between the Psychological well-being and Transmissibility factors. The highest correlation of this item with other items in the Psychological well-being was: "I feel my life is less enjoyable because of hepatitis B" (r = 0.528). Regarding these findings, it seemed that our patients' main concern was less enjoyable life because of difficult sex rather than the transmission of the virus to another person. Since correlation is not necessarily indicative of causation, such interpretation is a hypothetical one and needs further investigation.

Vitality highly correlated with IFS and PCS scores showing that this scale is mainly a measure of somatic aspect of the quality of life. High relation between Vitality and Depression scores may indicate a high relation between depression and somatization, particularly in Iranian patients.[30] As mentioned previously, somatic symptoms may be of major importance in patients with low educational levels. This may be the reason why our low-level educated patients had more impaired Vitality scores than the patients with high-levels of education.

Low Cronbach's α of the Vulnerability subscale can be interpreted in several ways. First, the low number of items in the subscales can affect this coefficient. Alternatively, it can reflect a low correlation between two items in the factor. Cronbach's α of less than 0.5 is considered unacceptable.[31] Because the Cronbach's α did not

reach the unacceptable threshold and because this item showed high discriminatory power, we retained it in the final analysis of the questionnaire. The Viral response item was created by developers of the questionnaire using the combination of Transmissibility and Vulnerability.[11] Although this item also showed discriminatory power in our study, this was a result of the Vulnerability factor rather than the whole subscale.

There are multiple liver (but not CHBV)-specific HRQOL instruments available in the literature.[9–11,32-34] The most important possible superiority of the HBQOL compared with other instruments is that it is CHBV-specific. Thereby as shown by Spiegel et al.[11] and the present study, HBQOL is more likely to detect changes in health status in this subset of patients. This may justify its use in clinical trials, although this statement definitely requires more evidence. Because of its nature (i.e., being disease-specific), HBQOL is unable to address HRQOL in patients with other diseases; thus it cannot be used for comparison among the patients with diseases other than CHBV. Table 6 provides a comparison between HBQOL and other liver disease-related instruments.

The present study had several strengths. The adequate sample size for this design minimized the probability of type II error, as mentioned in Materials and Methods. The adequate sample size was also confirmed by Bartlett's test of sphericity and the KMO test. Supervision to ensure completion of questionnaires additionally strengthened our study. Another advantage of our study was the comparison of HBQOL and its subscales with several instruments that measured similar constructs, to ensure its convergent validity as well as the use of different constructs to ensure divergent validity. Exhaustive construct validation in the present study together with the extensive content validation process performed in the study by Spiegel et al.[11] provided substantial evidence for the validity of HBQOL. Moreover, both studies showed the HBQOL to be reliable in most of its dimensions by test-retest and Cronbach's α.

Our study had also some limitations. The cross-sectional design did not allow us to measure the change in the scores of HBQOL (i.e., responsiveness testing). Regarding generalizability, although the study was undertaken in one clinic, the sample size of this study could be considered a representative of Iranian patients, both because diverse ethnic groups live in Tehran and because our clinic is a referral center that accepts patients from throughout Iran.[14]

Conclusion

The Iranian version of HBQOL v1.0 is a psychometrically sound measure with acceptable validity, reliability, and factor structure and can distinguish between different clinical conditions. Further studies for longitudinal assessment of this instrument, particularly in clinical trials, are warranted. In addition, studies in other cultures and languages can generalize the administration of HBQOL as a useful tool to assess the HRQOL in patients with CHBV.

Acknowledgement

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A view of Persepolis – Achaemenid Empire (c.550 – 331 BCE), around 60 Km northeast of Shiraz-Iran (Photo by M.H. Azizi MD)