Is there an association between Health Related Quality of Life, socio-demographic status and Fatigue in Patients with Chronic Hepatitis B?

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Abstract

***Background* : Chronic hepatitis B CHB) is a serious and prevalent disease which may negatively influence health related quality of life (HRQOL) and fatigue. The aim of the present study was to examine the relationship between demographic variables, HRQOL, and fatigue.**

***Methods :* A cross-sectional study was conducted involving 418 Iranian patients with CHB (average age 44.1 years, majority males). Participants completed a multidimensional fatigue inventory, chronic liver disease questionnaire, Euro quality of life-five dimensions questionnaire, and demographic information. Bivariate analyses were conducted using the Spearman correlation and Mann-Whitney U test. Hierarchical logistic regression modeling identified independent predictors of fatigue.**

***Results :* The most prevalent problems related to HRQOL were anxiety/depression and pain/discomfort. Except for reduced motivation other dimensions of fatigue were significantly higher among those with CHB compared to healthy controls ($p<0.05$). Age, sex, education, employment, disease stage and all HRQOL subscales were significantly related to fatigue level. The Nagelkerke R Square for the logistic regression model was 0.542.**

***Conclusions*: Poor HRQOL and fatigue are widespread among patients with CHB. Given these associations between demographic, psychological, and other HRQOL dimensions and fatigue, interventions that address these factors may help to reduce fatigue in patients with CHB.** (Acta gastroenterol. belg., **2017**, 80, **229-236**).

Keywords: chronic hepatitis B, fatigue, health related quality of life

Introduction

Hepatitis B infection is among the top 10 leading causes of death worldwide (1). International reports suggest that there have been more than 2 billion cases and of those, 400 million suffer from chronic hepatitis B (CHB) (2). Regions such as North America, Western Europe and Australia have been classified as areas of low CHB prevalence, whereas developing regions such as countries in Asia or Africa are high prevalence (1,3). There are between 1.5 and 2.5 million patients with CHB living in Iran (4). This country located in a miso-endemic region has a CHB prevalence of 2% to 7% (5).

Between 3% and 5% of people infected with the hepatitis B virus progress to the chronic form (2). CHB patients experience many complications such as cirrhosis, hepatocellular carcinoma, and liver failure (6). Physical symptoms include itching (pruritus), anorexia, icterus, and pain, as well as conditions such as depression, anxiety, and memory loss (2,7,8). These symptoms and syndromes have a negative impact on the health related quality of life (HRQOL) of CHB patients. HRQOL is important in chronic disorders because it serves as an indicator of health service needs and of the effectiveness of medical interventions. Studies indicate that HRQOL decreases as CHB disease advances in severity (9,10).

Fatigue is also a distressing symptom among patients with liver diseases and may be considered an important outcome measure (11). Fatigue is defined as a strong and durable sense of exhaustion unrelieved by resting that reduces capacity for mental and physical activity (12). Like HRQOL, fatigue is a multidimensional concept contributing to the behavioral and psychological aspects of the disease (13). Many studies confirm the important role that fatigue plays in chronic disorders such as viral hepatitis (14,15). The effect of fatigue on HRQOL in several chronic conditions has been examined (16,17). However, the association between these two biopsychosocial indicators has not been adequately studied in CHB patients.

Many clinical factors may influence fatigue. However, differences in social, demographic, cultural and lifestyle factors in different regions may also affect fatigue levels. Previous studies have shown that depression, sleep quality, self-efficacy, stress, sex, and social support are determinants of fatigue in chronic conditions (18-20). To our knowledge, however, factors related to fatigue in CHB patients have not yet been explored.

The objectives of the present study are to assess HRQOL and fatigue in patients with chronic hepatitis B infection, and to identify socio-demographic and health related factors that are associated with fatigue in CHB patients.

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Methods

Design and participants

A cross-sectional study was conducted between July and September 2015 in the Iran's Tehran Hepatitis Center, the national hepatitis center with the highest number of admissions for hepatitis in the country. A consecutive sample of 418 CHB outpatients was recruited. Based on a power of 80% and a two-tailed significance level (α) of 0.05 with an effect size (d) of 0.20, this number represents an adequate sample size for identifying correlates. Criteria for inclusion were a diagnosis of chronic hepatitis B infection based on international guidelines (21), age 18 years or older, and the absence of co-existing viral hepatitis or encephalopathy. Excluded were patients with severe psychological problems, those who spoke languages other than Persian, and those having co-morbid disorders such as stroke, heart disease, uncontrolled diabetes mellitus, or tuberculosis. Face-to-face interviews were conducted by trained researchers. The study was approved by the Institutional Review Board of Baqiyatallah University of Medical Sciences and all patients provided informed consent prior to data collection.

Reference group

To compare level of fatigue with a healthy population, we used data from an unpublished study which collected data on fatigue using the same measure used in the present study from 178 healthy individuals in Qazvin, Iran (approximately 90 miles from Tehran). The mean age of participants in the Qazvin study was 41.2 (SD, 6.3) and more than half were male. Approximately four-fifth of participants had university education and all were employed. This study was conducted to identify factors associated with fatigue among administrative staff at Qazvin University of Medical Sciences one year before our study (22).

Measures

Demographic information on age, sex, marital status, education, employment was collected on all participants. Health related variables such as body mass index (BMI), disease stage, comorbidity, and duration of disease were also recorded. Generic and specific HRQOL as well as fatigue were measured using the following questionnaires.

EuroQol five-dimension (EQ-5D)

The EQ-5D measures general HRQOL in two sections. The first section includes items that assess mobility, self-care, regular activities, pain or discomfort, and anxiety or depression. Each item has three response options from no problem (1) to severe (3). Scores from this section can be converted to a single utility index ranging from -0.594 to 1. Higher scores indicate better HRQOL. The second section is a visual analogue scale that participants rate their health status on a scale from 0 (worst imaginable health) to 100 (best imaginable health). The EQ-5D has been used previously in patients with hepatitis B (23).

Chronic liver disease questionnaire (CLDQ)

This is a disease-specific HRQOL measure for patients with liver disease. The 29-item CLDQ assesses six domains: abdominal symptoms, systemic symptoms, activity, fatigue, emotions, and worry. Response options for each item range from 1 (permanent problem) to 7 (not permanent problem) with lower scores indicating poorer HRQOL. Total score may be calculated by summing the mean score of individual domains. The Persian version of CLDQ has been used in several studies of patients with hepatitis B infection (24).

Multidimensional Fatigue Inventory (MFI)

The 20-item MFI assesses five dimensions of fatigue including general fatigue, physical fatigue, mental fatigue, reduced motivation, and reduced activity (4 items per dimension, ranging from 1 [true] to 5 [not true]). Each dimension yields a score from 4 to 20 with higher scores indicating greater fatigue. Although examining the total fatigue score is not recommended, it may be computed by summing scores for each dimension. The Persian version of the MFI has been previously validated among CHB patients (25).

Data analysis

Descriptive statistics with means and standard deviations for continuous variables and percentages for categorical variables were calculated (Tables 1 and 2). Differences between the study group and healthy controls in terms of demographics and fatigue subscales were first assessed by chi square and independent t-tests (Table 1). In order to improve comparison between domains of fatigue between these two groups, a general linear model was used to control for demographical factors. To identify significant correlates, associations between socio-demographic, health-related variables, and fatigue were determined in bivariate analyses. Mann-Whitney U test or Kruskal-Wallis and Spearman correlations were used to assess these associations (Table 3). Non-parametric tests were used because data were generally ordinal in nature and Kolmogorov-Smirnov test did not demonstrate normality ($p<0.05$). Significant correlates ($p<0.05$) in bivariate analyses were examined in multivariate analysis. Logistic regression was used to determine independent correlates of fatigue (Table 4). The median scores for the fatigue scale and its subscales were calculated and the variable was dichotomized into low and high scores at the median for examination in logistic regression models using the method described by Ericsson *et al*. (22) This strategy was

Table 1. — **Characteristics of the study sample and healthy controls**

Characteristics	CHB patients (n=418), mean (SD)/n (%)	Healthy controls (n= 178), mean (SD)/n (%)	P value
Gender			
Male	323 (77.3)	102 (57.3)	P< 0.001
Female	95 (22.7)	76 (42.7)	
Age (year)	44.12 (11.48)	41.18 (6.33)	P<0.01
Education			
Primary	30 (7.2)	0 (0)	P<0.001
Secondary	82 (19.6)		
High school	135 (32.3)	37 (20.8)	
University	171 (40.9)	141 (79.2)	
Employment			
Employed	236 (56.5)	178 (100)	P<0.001
Not employed	113 (27.0)	0 (0)	
Homemaker	69 (16.5)	0 (0)	
Marital status			
Single	43 (10.3)	26 (14.6)	0.161
Married	375 (89.7)	152 (85.4)	
Concomitant disease		NA	
Yes	126 (30.1)	-	NA
No	292 (69.9)	-	
BMI (Kg/m^2)	25.89 (3.89)	25.36 (2.93)	0.103
Treatment duration (year)	13.00 (7.67)	NA	NA
Disease stage		NA	
Non-cirrhotic	345 (82.9)	-	NA
Compensated cirrhosis	64 (15.3)	-	
Decompensated cirrhosis	9 (2.2)	-	
MFI subscales			
General fatigue	10.38 (4.29)	7.98 (3.23)	<0.001
Physical fatigue	9.24 (3.69)	7.36 (3.18)	<0.001
Mental fatigue	9.69 (3.78)	7.03 (3.12)	<0.001
Reduced activity	9.35 (3.74)	6.93 (3.25)	<0.001
Reduced motivation	7.50 (2.53)	6.68 (2.76)	<0.001

NA, not applicable

used because examining the total score for this fatigue scale is not recommended. A dummy system of coding was assigned to categorical variables: sex (male=0, female=1), education (high school=0, university=1), employment (not employed=0, employed=1), co-morbid physical disease (no=0, yes=1), and disease stage (non-cirrhotic=0, cirrhotic=1). Other predictors were left as continuous variables: age, BMI, treatment duration, and questionnaire subscales. For hierarchical logistic regression (Table 4 and 5), the following blocks of variables were entered into models: demographics (i.e., age, sex, education, and employment), clinical variables (i.e., co-morbid diseases, BMI, treatment duration, and CHB disease stage), EQ-5D dimensions (i.e., mobility, usual activity, pain/discomfort, anxiety/ depression, and EQ-VAS), and CLDQ dimensions (i.e., abdominal symptoms, systemic symptoms, activity, emotional function, and worry). Variables were categorized based on their theoretical considerations. Blocks of variables were entered in different orders to identify the best order with the highest predictability. Significance level was set at $p<0.05$ (two-tailed). All analyses were conducted by SPSS for Windows version 20.

Results

The average age of participants was 44.1 (SD, 11.5) and the majority (77.3%) were male. Less than half of respondents had a university education (40.9%) and more than half were employed (56.5%). Nearly 70% of

Table 2. — **Health related quality of life (CLDQ) and health status (EQ-5D & EQ-VAS) in the study group (n=418)**

	Mean	Standard deviation	Range
CLDQ			
Abdominal symptoms	6.06	1.17	1.00-7.00
Fatigue	5.57	1.22	2.20-7.00
Systemic symptoms	5.97	1.10	1.80-7.00
Activity	5.88	1.35	1.00-7.00
Emotional function	5.61	1.20	1.25-7.00
Worry	5.60	1.60	1.00-7.00
EQ-5D			
Utility score	0.873	0.158	-0.01-1.00
EQ-VAS	71.65	20.39	0-100

the participants had no co-morbidity besides CHB and only 17.5% were in the cirrhotic stage. Comparisons between our sample and the healthy controls indicated that there were significant differences between groups in terms of gender, age, education level, and employment. All fatigue (MFI subscales) scores were higher in the CHB sample compared to the healthy controls ($p<0.001$) (Table 1). After controlling for demographical variables (age, gender, education, and employment), except for reduced motivation ($p=0.094$) all other domains of fatigue remained significantly different between the study group and healthy controls ($p<0.05$).

Table 2 describes the health related quality of life measures (CLDQ and EQ-5D). In terms of disease-specific HRQOL, all domains of the CLDQ had similar scores. The domain with the highest score was abdominal symptoms with a mean of 6.06 (SD, 1.17). The EQ-5D utility index, as a measure of general HRQOL, had an average score of 0.87 (SD, 0.16), and the EQ-VAS had a mean score of 71.6 (SD, 20.4). As noted in Figure 1, the most common complaints were anxiety/depression, pain/discomfort, and problems with mobility.

Table 3 presents the bivariate relationships between the study variables and fatigue subscale scores. Significant associations were found between almost all variables and at least one aspect of fatigue, with the exception of marital status. Among demographics, sex and employment were related to all fatigue dimensions, whereas among clinical variables, participants' BMI, treatment duration and disease stage were only weakly associated with fatigue subscales. All subscales of the EQ-5D and CLDQ were significantly associated with fatigue scores ($p<0.001$).

Tables 4 and 5 present results from regression models. Odds ratios were higher than 2.0 for females compared to males in term of general fatigue, physical fatigue, reduced activity, and reduced motivation. Cirrhotic patients were at greater risk of general (OR=2.3) and physical fatigue (OR=3.3) compared to non-cirrhotic patients. Non-cirrhotic patients were also much less likely to have fatigue on the CLDQ scale (OR=0.28) compared to cirrhotic patients. Higher scores on several EQ-5D subscales were associated with increased fatigue. In particular, patients with higher anxiety or depression scores experienced much more fatigue than others ($p<0.001$). Lower CLDQ subscale scores for several domains were also associated with a greater risk of fatigue. With total MFI score as the dependent variable, significant predictors were sex, education, employment, comorbidity, disease stage, and several EQ-5D and CLDQ domains. For the EQ-5D and CLDQ domains, the only significant predictors were usual activity, EQ-VAS, abdominal symptoms, emotional function and worry. The Nagelkerke R Square was 0.542.

Discussion

We examined associations between demographic, clinical, and quality of life characteristics and fatigue in patients with CHB. Our findings indicated that age, sex, education, employment, comorbidity, and stage of disease are associated with fatigue.

There are many studies that have evaluated the HRQOL among patients with CHB. In a study of Chinese patients that examined both general and disease-specific measures of the HRQOL (i.e., SF-36 and CLDQ), researchers reported lower scores in CHB patients compared to controls, especially in patients with cirrhosis (9). We also found higher levels of fatigue in cirrhotic patients compared to those without cirrhosis. Drazic and Caltabiano found that HRQOL among patients with hepatitis B was similar to that of patients with hepatitis C infection and both had poor HRQOL compared to patients without hepatitis (26).

There is only limited research on fatigue among patients with CHB and most of the existing studies focused only on patients with hepatitis C infection. For

Table 3. — **Associations between fatigue dimensions, socio-demographic, and health related variables in the study group)**

	n	General fatigue	Physical fatigue	Mental fatigue	Reduced activity	Reduced motivation	Fatigue of CLDQ
Age [a]	418	0.002	0.133**	0.005	0.131**	0.024	-0.002
Sex [b]							
Male	323	9.77 (4.07)***	8.73 (3.71)***	9.29 (3.68)***	8.69 (3.54)***	7.22 (2.53)***	5.70 (1.14)***
Female	95	12.47 (4.38)	10.97 (3.07)	11.08 (3.79)	10.67 (4.10)	8.44 (2.31)	5.12 (1.37)
Marital status [b]							
Single	43	9.81 (4.55)	8.39 (3.30)	10.11 (4.03)	9.13 (2.88)	8.09 (2.45)	5.67 (1.12)
Married	375	10.45 (4.25)	9.34 (3.73)	9.65 (3.75)	9.37 (3.83)	7.43 (2.53)	5.56 (1.23)
Education [b]							
High school or lower	247	10.78 (4.46)*	9.49 (3.82)	10.11 (3.97)**	9.89 (3.99)**	7.39 (2.47)	5.55 (1.31)
University	171	9.81 (3.97)	8.88 (3.49)	9.09 (3.40)	8.56 (3.20)	7.65 (2.61)	5.59 (1.08)
Employment [c]							
Employed	236	9.60 (3.97)***	8.49 (3.50)***	9.07 (3.46)***	8.58 (3.14)***	7.21 (2.48)**	5.69 (1.13)*
Not employed	113	10.58 (4.21)	9.77 (4.00)	9.91 (3.95)	10.07 (4.08)	7.65 (2.72)	5.61 (1.15)
Homemaker	69	12.73 (4.60)	10.94 (3.11)	11.47 (3.98)	10.79 (4.39)	8.23 (2.23)	5.08 (1.51)
Concomitant disease [b]							
No	292	10.19 (4.34)	8.93 (3.72)**	9.52 (3.76)	9.08 (3.21)	7.40 (2.54)	5.65 (1.20)*
Yes	126	10.84 (4.14)	9.96 (3.55)	10.10 (3.80)	9.96 (4.54)	7.73 (2.50)	5.38 (1.24)
BMI (Kg/m^2) [a]	418	0.068	0.025	0.100*	0.038	-0.021	-0.040
Treatment duration (year)[a]	418	0.032	0.142**	0.062	-0.029	-0.013	0.000
Disease stage [b]							
Non-cirrhotic	345	10.17 (4.30)*	8.96 (3.59)**	9.63 (3.79	9.27 (3.71)	7.46 (2.52)	5.71 (1.17)***
Others	73	11.39 (4.08)	10.47 (3.94)	10.01 (3.74	9.72 (3.90)	7.69 (2.59)	4.90 (1.24)
EQ-5D dimensions [a, §]							
Mobility	418	0.297**	0.286**	0.141**	0.089	0.096	-0.0232**
Usual activity	418	0.277**	0.224**	0.155**	0.215**	0.121*	-0.260**
Pain/discomfort	418	0.325**	0.312**	0.251**	0.102*	0.139**	-0.385**
Anxiety/depression	418	0.549**	0.497**	0.478**	0.299**	0.244**	-0.542**
EQ-5D utility score [a]	418	-0.578**	-0.526**	-0.454**	-0.261**	-0.261**	0.594**
EQ-VAS [a]	418	-0.558**	-0.497**	-0.402**	-0.288**	-0.274**	0.495**
CLDQ dimensions (excepted for fatigue)[a]							
Abdominal symptoms	418	-0.367**	-0.424**	-0.324**	-0.225**	0.226**	0.480**
Systemic symptoms	418	-0.529**	-0.477**	-0.296**	-0.322**	-0.262**	0.629**
Activity	418	-0.493**	-0.499**	-0.330**	-0.225**	-0.244**	0.606**
Emotional function	418	-0.699**	-0.606**	-0.581**	-0.455**	-0.467**	0.757**
Worry	418	-0.430**	-0.359**	-0.299**	-0.269**	-0.310**	0.403**

*p<0.05 ; **p<0.01 ; ***p<0.001 ; n, number of participants (correlations were computed with n=418) ; Bivariate analysis: a, Spearman correlation (r) ; b, Mann-Whitney U test M (SD), and c, Kruskal-Wallis test M (SD) ; §, because the self-care dimension had no any reported problem it has been omitted from EQ-5D dimensions

Table 4.— **Hierarchical logistic regression for associations between demographic and health variables on fatigue dimensions in the study sample**

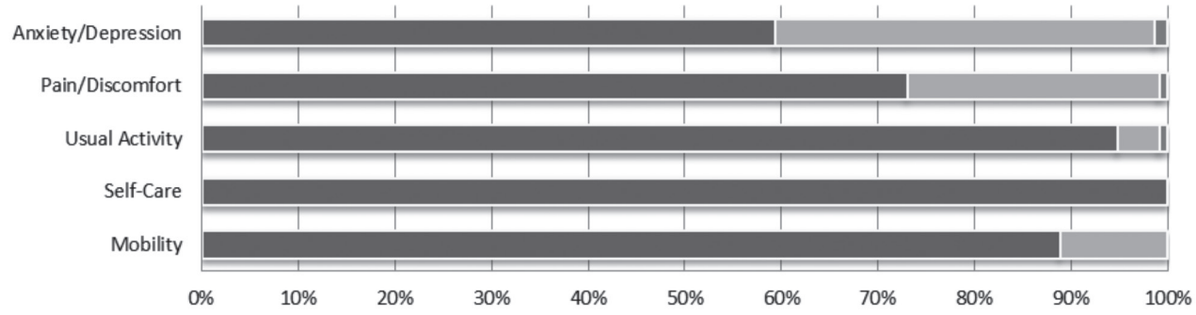
Independent variables	Dependent variables					
	General fatigue>10 OR (95% CI)	Physical fatigue> 9 OR (95% CI)	Mental fatigue> 9 OR (95% CI)	Reduced activity> 9 OR (95% CI)	Reduced motivation>7 OR (95% CI)	Fatigue of CLDQ>5.80 OR (95% CI)
Demographics						
Age (year)	-	1.02 (1.00-1.04)*	-	1.02 (1.00-1.04)*	-	-
Sex	2.13 (1.25-3.62)**	2.70 (1.53-4.75)**	1.42 (0.84-2.40)	2.15 (1.22-3.80)**	2.81 (1.64-4.80)***	0.65 (0.34-1.10)
Education	0.77 (0.51-1.15)	-	070 (0.47-1.04)	0.66 (0.44-1.00)	-	-
Employment	0.65 (0.42-1.01)	0.61 (0.38-0.98)*	0.74 (0.48-1.14)	0.77 (0.48-1.25)	1.00 (0.65-1.57)	0.94 (0.61-1.45)
Clinical var.						
Concomitant disease	-	1.15 (0.71-1.86)	-	-	-	0.75 (0.48-1.18)
BMI (Kg/m2)	-	-	1.02 (0.97-1.07)	-	-	-
Treatment duration (year)	-	1.04 (1.01-1.07)**	-	-	-	-
Disease stage	2.31 (1.35-3.95)**	3.31 (1.86-5.92)***	-	-	-	0.28 (0.15-0.50)***
EQ-5D dimensions						
Mobility	3.14 (1.28-7.72)*	2.32 (0.92-5.83)	1.09 (0.50-2.36)	-	-	0.18 (0.05-0.60)**
Usual activity	12.63 (1.50-105.93)*	2.12 (0.55-8.20)	0.82 (0.32-2.10)	7.43 (1.60=34.48)*	3.67 (1.16-11.63)*	0.00 (0.00)
Pain/discomfort	1.48 (0.83-2.64)	1.00 (0.55-1.81)	1.81 (1.04-3.17)*	0.77 (0.47-1.27)	1.18 (0.73-1.93)	0.30 (0.16-0.59)***
Anxiety/depression	2.56 (1.56-4.18)***	3.67 (2.21-6.12)***	4.37 (2.69-7.11)***	2.17 (1.37-3.43)**	1.49 (0.96-2.32)	0.26 (0.15-0.45)***
EQ-VAS	0.96 (0.95-0.97)***	0.97 (0.96-0.98)***	0.98 (0.96-0.99)**	0.99 (0.98-1.00)	0.99 (0.98-1.00)	1.03 (1.01-1.04)***
CLDQ dimensions						
Abdominal symptoms	0.87 (0.65-1.16)	0.69 (0.52-0.93)*	0.55 (0.42-0.73)***	0.67 (0.52-0.86)**	0.75 (0.59-0.95)*	2.10 (1.43-3.08)***
Systemic symptoms	0.91 (0.62-1.31)	0.50 (0.33-0.77)**	1.63 (1.14-2.33)**	0.83 (0.62-1.20)	0.90 (0.68-1.84)	1.35 (0.86-2.14)
Activity	0.82 (0.64-1.05)	0.72 (0.54-0.96)*	1.13 (0.88-1.45)	1.46 (1.16-1.84)**	1.08 (0.88-1.34)	1.40 (1.01-1.92)*
Emotional function	0.40 (0.27-0.58)***	0.57 (0.38-0.85)**	0.45 (0.32-0.64)***	0.39 (0.28-0.54)***	0.46 (0.33-0.63)***	4.40 (2.70-7.18)***
Worry	0.88 (0.73-1.08)	1.22 (0.98-1.53)	1.03 (0.858-1.25)	1.16 (0.96-1.39)	1.12 (0.95-1.32)	0.89 (0.71-1.13)

*p<0.05 ; **p<0.01 ; ***p<0.001 ; OR, odds ratio ; CI, confidence interval ; Nagelkerke R Square range: 0.239 (Reduced motivation) to 0.662 (Fatigue of CLDQ)

example, Karaivazoglou *et al*. examined 45 patients with CHB, finding a close association between fatigue and several physical components of the HRQOL (15). These results were similar to our finding that physical activity level, pain, and other physical health components of HRQOL were related to general and physical fatigue. Karaivazoglou *et al* also reported psychological impairments among CHB patients with fatigue (15).

Assessment of mental health is a crucial issue among those with life-threatening conditions. Although infection with the Hepatitis B virus may be curable if treatment is provided at an early stage of the disease, the mortality rate is still high (27). Social stigmatization due to the disease, problems in daily life, and restrictions on social activities may lead to poor mental health, anxiety and depression (26). To date, many studies have investigated the mental health of patients with viral hepatitis and most have reported serious problems in this regard (15,28). One study found that more than 90% of patients with CHB may be at risk of depression, known to be related to lower HRQOL (7). We also found that depression or anxiety was frequent in CHB patients and these symptoms were closely related to each of the fatigue subscales in logistic regression models.

Factors such as age, sex, education, employment, concomitant disease, disease stage and several HRQOL



	Mobility	Self-Care	Usual Activity	Pain/Discomfort	Anxiety/Depression
No problem	371	418	396	305	248
Some problems	47	0	18	109	164
Extreme problems	0	0	4	4	6

Fig. 1. — Distribution of EQ-5D dimensional frequency in the study sample (n-418)

dimensions have also been linked to several components of fatigue by other investigators. For example, Teuber *et al*. in a study of patients with hepatitis C found that age was related to quality of life and fatigue in these patients. Patients who were older reported higher levels of fatigue and reported poorer health status (29). In another study, education level was positively associated with HRQOL among patents with CHB (30). Other risk factors for poor HRQOL among such patients reported in the literature include an introverted personality style, social incompetence, severe overall illness, lower economic status, and abnormal liver function tests (9,31). Pain and physical activity level in patients with hepatitis C have been strong predictors of HRQOL in other study, although have less frequently been examined in patients with CHB (32).

Another finding of the current study is the multidimensional nature of fatigue. We conducted two series of logistic regression models, first considering individual aspects of fatigue, and then examining fatigue as a unidimensional concept (i.e., total score). When the fatigue measure was broken down into subscales, associations between variables were clearer. Examining only the total score for overall fatigue may conceal important relationships. Our results support the recommendations suggested by the original author of the MFI that it was important to consider individual aspects of fatigue to better understand its relationship to chronic health problems (13).

Several limitations of the present study should be considered. First, this was a convenience sample of CHB patients and so the findings cannot be generalized to all patients with CHB in Iran. However, our power analysis indicated that our sample size for statistical analyses was more than adequate. Second, this was a cross-sectional study that did not provide information on direction of causation between the associations identified. Nevertheless, given that this study was an initial effort to assess fatigue and related factors among patients with CHB in Iran, it may provide a foundation for future research in this area. Third, many other demographic and clinical factors may contribute to fatigue in such patients beyond those identified in the present study. However, the variables measured here produced a considerable value for Nagelkerke R Square, suggesting that we identified many of the major components. Finally, this is the first report that has compared levels of fatigue in Iranian CHB patients to healthy individuals, even though that population was from a different location in Iran (although near Tehran). This comparison, however, may provide a better understanding of how fatigue affects patients with CHB compared to other populations.

Conclusions: The present study found that HRQOL among patients with CHB is often compromised, and that these patients may experience higher levels of fatigue than healthy individuals living in the community. Knowing that factors such as age, sex, education, employment and severity of disease predict higher levels of fatigue in such patients may help to guide strategies for managing disease in these patients and for developing new interventions that improve quality of life. Moreover, triaging patients based on those who may be at higher risk for fatigue may be helpful in preventing further declines in quality of life. Those at greatest risk for fatigue appear to be CHB patients with poorer mental health and lower levels of physical activity, suggesting that interventions should target these areas in particular. Further research is needed to better understand the causal direction of these associations and how fatigue affects and is affected by demographic, psychological, and physical health characteristics of patients with CHB in different cultural settings.

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Conflict of interests

The authors declare that they have no conflict of interests.

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