Gastroenterology Report, 2024, **12**, goae015
https://doi.org/10.1093/gastro/goae015
Original Article

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Health-related quality of life in Thai patients with chronic hepatitis B

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Abstract

Background: Chronic hepatitis B (CHB) significantly impacts the health-related quality of life (HRQoL), but remains underexplored in the Thai population. Health state utilities (HSU) are indicators reflecting HRQoL which serve as fundamental inputs for economic evaluation analyses. This study aimed at assessing differences in HRQoL across five CHB stages in Thai patients, including non-cirrhotic CHB, compensated cirrhosis, decompensated cirrhosis, early-/intermediate-stage hepatocellular carcinoma (HCC) and advanced-/terminal-stage HCC.

Methods: We conducted a cross-sectional study to collect HRQoL data from patients with CHB at five stages. The study included patients with CHB who were followed up at a super-tertiary care centre between March 2021 and February 2022. The participants completed the EQ-5D-5L questionnaire and provided demographic data. Disease stage and relevant data were obtained from medical records. HSU and Euroqol-visual analogue scale (EQ-VAS) scores, calculated using Thai-specific conversion coefficients, were assessed.

Results: Among 422 patients, 236 did not have cirrhosis, 92 had compensated cirrhosis, 13 had decompensated cirrhosis, 55 had early-/intermediate-stage HCC, and 26 had advanced-/terminal-stage HCC. The HSU scores for non-cirrhotic, compensated cirrhosis, decompensated cirrhosis, early-/intermediate-stage HCC and advanced-/terminal-stage HCC were 0.95 ± 0.08, 0.89 ± 0.16, 0.79 ± 0.19, 0.89 ± 0.12 and 0.52 ± 0.39, respectively. Similarly, the EQ-VAS scores for various CHB stages were 83.56 ± 12.90, 80.48 ± 13.03, 68.76 ± 17.40, 79.00 ± 14.38 and 62.92 ± 20.62, respectively. A significant correlation ($r = 0.469$, $P < 0.001$) was observed between the HSU and EQ-VAS scores. The disease progression led to a notable HSU decline, particularly in the advanced-/terminal-stage HCC group (regression coefficient: –0.436, $P < 0.001$). The EQ-VAS scores indicated reduced quality of life in advanced liver disease.

Conclusions: Later CHB stages compromise the HRQoL. Decompensated cirrhosis and advanced-/terminal-stage HCC profoundly affect physical health and quality of life, whereas patients with compensated cirrhosis and early-/intermediate-stage HCC report better HRQoL.

Keywords: health state utilities; chronic hepatitis B; health-related quality of life; EQ-5D-5L

Introduction

Hepatitis B virus (HBV) is a partially double-stranded DNA virus that replicates through the formation of covalently closed circular DNA in infected hepatocytes [1]. In Asian countries, vertical maternal-to-child transmission is the main route of infection with most of the HBV-infected infants developing chronic hepatitis B (CHB) if they did not receive the HBV vaccines [2]. Adults may also be infected with HBV by other means, such as blood-borne and sexually transmitted infections.

Globally, approximately 296 million people suffer from CHB, and 1.5 million new HBV infections are reported annually; these infected people are at high risk of developing CHB [3, 4]. Southeast Asia region has a moderate to high prevalence of HBV infection [5], particularly in Thailand, with a prevalence of 5.1%, accounting for 3 million people with CHB [6]. A recent study reported that, despite the implementation of the expanded program on immunization in recent decades, 2.9% of individuals who underwent health check-ups in Thailand had CHB and 27.8% had evidence of past HBV infection. In addition, the study indicated that CHB remains a significant challenge in Thailand [7]. CHB is associated with the progression of liver cirrhosis, hepatocellular carcinoma (HCC) and death [1, 8].

Received: 13 June 2023. **Revised:** 3 January 2024. **Accepted:** 20 February 2024

CHB is among the major health concerns in Thailand [6, 9]. Thus, measuring the health-related quality of life (HRQoL), that can determine the disease burden, is beneficial for the further evaluation of the health economic status [10, 11]. Health state utility (HSU) values are required to calculate the quality-adjusted life years. Healthy individuals in Thailand have been reported to have an HSU value of 0.93 ± 0.10 [12]. However, the effect of CHB on HRQoL remains unknown in Thailand. We hypothesize that HSU values may vary among patients with CHB at different stages.

This study aimed to determine the differences in HRQoL at each CHB stage, namely non-cirrhotic CHB, compensated cirrhosis [cirrhosis with Child-Turcotte-Pugh (CTP) A, decompensated cirrhosis (cirrhosis with CTP B and C], early-/intermediate-stage HCC [Barcelona Clinic Liver Cancer (BCLC) stage 0-B] and advanced-/terminal-stage HCC (BCLC stage C/D) in Thai patients.

Methods

Study participants

This was a cross-sectional study. We prospectively enrolled patients aged ≥18 years who were diagnosed with CHB and HBV-related HCC between March 2021 and February 2022 and who were regularly followed up at Songklanagarind Hospital (Hat Yai, Thailand), a super-tertiary centre in Southern Thailand.

CHB was defined as the presence of hepatitis B virus surface antigen twice within a 6-month interval [13–15]. HCC diagnosis was confirmed either by histology or typical imaging diagnostic criteria according to the international practice guidelines [16–18]. The Barcelona Clinic Liver Cancer (BCLC) staging system was used to classify patients with HCC into early-/intermediate-stage (BCLC stage 0–B) and advanced-/terminal-stage HCC (BCLC stage C/D) [19]. Compensated cirrhosis was defined as asymptomatic cirrhosis with CTP A (score, 5–6). Decompensated cirrhosis was defined as the presence of cirrhotic complications, including jaundice, ascites, spontaneous bacterial peritonitis, variceal bleeding, or hepatic encephalopathy, with CTP B (score, 7–9) or CTP C (score, 10–15) [20].

The exclusion criteria for the study were as follows: (1) patients co-infected with other types of viral hepatitis; (2) patients with human immunodeficiency virus; (3) patients with other causes of cirrhosis; and (4) patients with other causes of HCC.

All participants were requested to self-answer a two-part questionnaire. A research assistant helped in clarifying any inquiries regarding the questionnaire to the participants. The questionnaire consists of two parts. The first part is the sociodemographic data questionnaire, i.e. sex, age, marital status, educational level and monthly income. The second part is the EQ-5D-5L, including the EQ-5D descriptive system and Euroqol-visual analogue scale (EQ-VAS).

Each participant was then classified into one of the five groups: (1) CHB in the absence of cirrhosis and HCC; (2) compensated cirrhosis (CTP A); (3) decompensated cirrhosis (CTP B and C); (4) early-/intermediate-stage HCC–BCLC stage 0, A, or B; and (5) advanced-/terminal-stage HCC–BCLC stage C or D. In patients having HCC and concurrent cirrhosis, the categorization was performed according to the HCC status.

EQ-5D-5L questionnaires and HSU calculations

The EQ-5D is a standardized instrument developed by the EuroQol Group to measure a patient's health status as a single index value. The EuroQol Group created a Thai version of the EQ-5D-5L for non-commercial use (https://euroqol.org/eq-5d-instruments/eq-5d-5l-about/). The investigators were granted permission to use the Thai version of the EQ-5D-5L (https://registration.euroqol.org/ with registration ID 38729). The EuroQoL Research Foundation allowed the use of the questionnaire for academic purposes.

The EQ-5D-5L is the five-level version of the EQ-5D, and it consists of two parts, the EQ-5D descriptive system and EQ-VAS [21].

The first part, the EQ-5D descriptive system, has five dimensions (mobility, self-care, usual activities, pain/discomfort and anxiety/depression). Each dimension has one standardized questionnaire with answers at five levels (no problems, slight problems, moderate problems, severe problems and extreme problems). The participants were asked to select the most appropriate statement reflecting their status for each of the five dimensions.

The second part, EQ-VAS, represents the respondent's health status using a vertical visual analogue scale (VAS) which is composed of a score rating in a continuous value range of 0 (worst imaginable health) to 100 (best imaginable health). The participants were asked to choose the most compatible score for their current health status based on their perception.

The values obtained from the EQ-5D-5L descriptive system were combined and calculated using the crosswalk function (http://www.hitap.net/documents/89762) with Thai coefficient values in each dimension to generate the HSU for each participant [22]. For example, if the participant provided the following answers: slight problem in mobility (Level 2), no problem in self-care (Level 1), slight problem in usual activities (Level 2), moderate problem in pain/discomfort (Level 3) and extreme problem in anxiety/depression (Level 5), the health state profile should be 2, 1, 2, 3 and 5. It can be calculated as 1 − 0.056 − 0 − 0.043 − 0.068 − 0.249 = 0.584 according to the aforementioned calculation guidelines. The best health state has a value of one, whereas the worst health state has a value of zero or below zero (negative value). The EQ-VAS score directly indicates the respondent's self-rated health on a 0–100 scale. A score of 100 implies that the patients had the best health status, while a score of 0 indicates that they had the worst health status.

The study protocol was approved by the Institutional Review Board and Ethics Committee of the Faculty of Medicine, Prince of Songkla University, Hat Yai, Thailand (REC: 63–368-14–1). This study was conducted in accordance with the ethical guidelines and principles outlined in the 1975 Declaration of Helsinki. All the patients who were invited to participate in the study could decide whether or not they want to answer the questionnaire; they provided their consent by voluntarily filling out the questionnaire. The need to document consent was waived.

Statistical analysis

Continuous variables were presented as mean ± SD. Categorical variables are expressed as numbers and percentages. The independent Student's *t*-test and rank-sum test were used to compare the continuous variables. Sex, marital status, occupation and education level were compared using the Chi-squared or Fisher's exact tests. Age, sex and marital status were adjusted for HSU and EQ-VAS scores using linear regression analyses. The normality test, using Shapiro–Wilk test and histograms were performed to assess the normal distribution of the HSU and EQ-VAS variables. Although these two variables were not normally distributed, the data were presented as mean ± SD in accordance with other literature reporting HSU and EQ-VAS [23, 24] and rank-sum test were used to compare them. Spearman's test of correlation was used to measure the strength of the relationship between the HSU and EQ-VAS. All statistical analyses were

performed using R software (version 4.2.3; R Foundation, Austria). Statistical significance was defined as a two-sided P-value < 0.05.

Results

A total of 422 eligible patients were recruited for this study. Patients were divided into five groups: (1) non-cirrhosis ($n = 236$); (2) compensated cirrhosis ($n = 92$); (3) decompensated cirrhosis ($n = 13$); (4) early-/intermediate-stage HCC ($n = 55$); and (5) advanced-/terminal-stage HCC ($n = 26$).

Baseline demographics

Table 1 summarizes the sociodemographic and clinical characteristics of the participants. The mean age of the entire cohort was 57.0 ± 12.5 years, and the patients with non-cirrhotic CHB were younger than those in the other groups ($P < 0.001$). The patients with early-/intermediate-stage HCC and advanced-/terminal-stage HCC had higher proportions of males than those in the non-cirrhotic group (81.8% *vs* 55.1%; $P < 0.001$ and 80.8% *vs* 55.1%; $P = 0.021$). The married status was predominant in all patients with CHB. The highest proportion of employment status was observed in patients with CHB without cirrhosis (80.1%) compared to the other groups ($P < 0.001$ in non-cirrhotic compared with compensated cirrhosis, decompensated cirrhosis and early-/intermediate-stage HCC group; $P = 0.01$ in non-cirrhotic compared with advanced-/terminal-stage HCC group). The unemployment rate showed a significant increase in the later stages of the disease, including decompensated cirrhosis (53.8%) and advanced-/terminal-stage HCC (30.8%). More than half of patients with CHB, with decompensated cirrhosis and HCC, had elementary school as their highest education level. In contrast, nearly half of the patients with CHB without cirrhosis had a bachelor's degree as their highest education level. The median monthly income of the non-cirrhosis group was the highest (25,000 Thai Baht; IQR, 12,000–39,910 Thai Baht).

EQ-5D-5L questionnaire

Table 2 presents the results of the analyses for each health dimension, including mobility, self-care, usual activities, pain/discomfort and anxiety/depression problems, in different CHB groups: non-cirrhosis, compensated cirrhosis, decompensated cirrhosis, early-/intermediate-stage HCC and advanced-/terminal-stage HCC.

Across the CHB stages, individuals with advanced-/terminal-stage HCC experienced the highest number of severe and extreme problems across all dimensions. The percentage of individuals with mobility problems increased significantly from the non-cirrhosis group (1.7% and 1.3% with moderate and severe problems, respectively) to the decompensated cirrhosis (30.8% with moderate problems) and advanced-/terminal-stage HCC (57.7% with moderate to extreme problems) groups. The percentage of individuals with self-care problems increased slightly in the compensated cirrhosis group (3% with moderate to extreme problems) and more significantly in the advanced-/terminal-stage HCC group (34.5% with moderate to extreme problems). The percentage of individuals with problems during usual activity increased from the non-cirrhosis group (1.3% with moderate to extreme problems) to the decompensated cirrhosis (23.1% with moderate to extreme problems) and advanced-/terminal-stage HCC (61.6% with moderate to extreme problems) groups. The percentage of individuals with pain/discomfort problems was the highest in the advanced-/terminal-stage HCC group (61.5% with moderate to extreme problems). The percentage of

Table 1. Baseline demographics stratified according to chronic hepatitis B groups

Characteristic	Non-cirrhosis ($N = 236$)	Compensated cirrhosis ($N = 92$)	Decompensated cirrhosis ($N = 13$)	Early- and intermediate-stage HCC ($N = 55$)	Advanced- and terminal-stage HCC ($N = 26$)
Age, years, mean (SD)	52.7 (11.8)	61.4 (10.9)	65.6 (11.2)	64.6 (11.1)	60.7 (11.3)
Male sex, *n* (%)	130 (55.1)	55 (59.8)	6 (46.2)	45 (81.8)	21 (80.8)
Marital status, *n* (%)					
Married	190 (80.5)	73 (79.3)	11 (84.6)	47 (85.5)	24 (92.3)
Single	33 (14.0)	8 (8.7)	0 (0.0)	1 (1.8)	0 (0.0)
Divorced	7 (3.0)	6 (6.5)	1 (7.7)	4 (7.3)	0 (0.0)
Widow/Widower	6 (2.5)	5 (5.4)	1 (7.7)	3 (5.5)	2 (7.7)
Employment, *n* (%)					
Employed	189 (80.1)	55 (59.8)	5 (38.5)	31 (56.4)	15 (57.7)
Unemployed	24 (10.2)	13 (14.1)	7 (53.8)	16 (19.1)	8 (30.8)
Retired	23 (9.7)	24 (26.1)	1 (7.7)	8 (14.5)	3 (11.5)
Education, *n* (%)					
Elementary school	35 (14.8)	25 (27.2)	9 (69.2)	31 (56.4)	16 (61.5)
High school	69 (29.2)	30 (32.6)	2 (15.4)	13 (23.6)	6 (23.1)
Bachelor's degree	105 (44.5)	31 (33.7)	1 (7.7)	8 (14.5)	4 (15.4)
Higher	27 (11.4)	6 (6.5)	1 (7.7)	3 (5.5)	0 (0.0)
Monthly income, THB, median (IQR)	25,000 (12,000, 39,910)	15,500 (6,500, 30,000)	3,000 (0, 9,800)	10,000 (0, 20,000)	6,500 (0, 15,000)
Treatment, *n* (%)					
No treatment	121 (51.3)	6 (6.5)	0 (0.0)	2 (3.6)	4 (15.4)
Lamivudine	29 (25.2)	29 (33.7)	4 (30.8)	28 (52.8)	14 (63.6)
Tenofovir	28 (24.3)	19 (22.1)	2 (15.4)	4 (7.5)	1 (4.5)
Entecavir	20 (17.4)	19 (22.1)	3 (23.1)	11 (20.8)	3 (13.6)
Tenofovir alafenamide	36 (31.3)	16 (18.6)	3 (23.1)	6 (11.3)	2 (9.1)
Telbivudine	1 (0.9)	0 (0.0)	0 (0.0)	1 (1.9)	0 (0.0)
Lamivudine + tenofovir	1 (0.9)	3 (3.5)	1 (7.7)	3 (5.7)	2 (9.1)

HCC, hepatocellular carcinoma; THB, Thai baht.
Means with standard deviations (SD) or medians with interquartile ranges (IQR) are presented for quantitative variables, whereas counts with proportions are presented for categorical variables.

Table 2. Analysis of each health dimension according to chronic hepatitis B groups

Health dimension	Non-cirrhosis (*N* = 236)	Compensated cirrhosis (*N* = 92)	Decompensated cirrhosis (*N* = 13)	Early- and intermediate-stage HCC (*N* = 55)	Advanced- and terminal-stage HCC (*N* = 26)
Mobility, *n* (%)					
No problem	207 (87.7)	63 (68.5)	5 (38.5)	39 (70.9)	7 (26.9)
Slight problem	22 (9.3)	20 (21.7)	4 (30.8)	9 (16.4)	4 (15.4)
Moderate problem	4 (1.7)	5 (5.4)	4 (30.8)	7 (12.7)	5 (19.2)
Severe problem	3 (1.3)	4 (4.3)	0 (0.0)	0 (0.0)	6 (23.1)
Unable/extreme problem	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	4 (15.4)
Self-care, *n* (%)					
No problem	231 (97.9)	84 (91.3)	12 (92.3)	51 (92.7)	13 (50.0)
Slight problem	2 (0.8)	5 (5.4)	1 (7.7)	2 (3.6)	4 (15.4)
Moderate problem	3 (1.3)	1 (1.1)	0 (0.0)	2 (3.6)	1 (3.8)
Severe problem	0 (0.0)	2 (2.2)	0 (0.0)	0 (0.0)	3 (11.5)
Unable/extreme problem	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	5 (19.2)
Usual activities, *n* (%)					
No problem	223 (94.5)	74 (80.4)	9 (69.2)	37 (67.3)	6 (23.1)
Slight problem	10 (4.2)	14 (15.2)	1 (7.7)	8 (14.5)	4 (15.4)
Moderate problem	3 (1.3)	2 (2.2)	1 (7.7)	7 (12.7)	4 (15.4)
Severe problem	0 (0.0)	1 (1.1)	2 (15.4)	1 (1.8)	6 (23.1)
Unable/extreme problem	0 (0.0)	1 (1.1)	0 (0.0)	2 (3.6)	6 (23.1)
Pain/Discomfort, *n* (%)					
No problem	146 (61.9)	31 (33.7)	3 (23.1)	24 (43.6)	3 (11.5)
Slight problem	76 (32.2)	50 (54.3)	3 (23.1)	22 (40.0)	7 (26.9)
Moderate problem	11 (4.7)	6 (6.5)	4 (30.8)	8 (14.5)	7 (26.9)
Severe problem	3 (1.3)	4 (4.3)	3 (23.1)	1 (1.8)	7 (26.9)
Unable/extreme problem	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	2 (7.7)
Anxiety/Depression, *n* (%)					
No problem	186 (78.8)	69 (75.0)	7 (53.8)	34 (61.8)	13 (50.0)
Slight problem	38 (16.1)	17 (18.5)	4 (30.8)	18 (32.7)	5 (19.2)
Moderate problem	12 (5.1)	3 (3.3)	1 (7.7)	2 (3.6)	5 (19.2)
Severe problem	0 (0.0)	3 (3.3)	1 (7.7)	1 (1.8)	3 (11.5)
Unable/extreme problem	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

HCC, hepatocellular carcinoma.

Table 3. Analysis of HSU and EQ-VAS scores according to chronic hepatitis B groups

Score	Non-cirrhosis (*N* = 236)	Compensated cirrhosis (*N* = 92)	Decompensated Cirrhosis (*N* = 13)	Early- and intermediate-stage HCC (*N* = 55)	Advanced- and terminal-stage HCC (*N* = 26)
HSU scores, mean (SD)	0.95 (0.08)	0.89 (0.16) $P < 0.001$	0.79 (0.19) $P < 0.001$	0.89 (0.12) $P < 0.001$	0.52 (0.39) $P < 0.001$
EQ-VAS scores, mean (SD)	83.56 (12.90)	80.48 (13.03) $P = 0.041$	68.76 (17.40) $P = 0.001$	79.00 (14.38) $P = 0.028$	62.92 (20.62) $P < 0.001$

HCC, hepatocellular carcinoma; SD, standard deviation. HSU, health state utility; EQ-VAS, Euroqol-visual analogue scale.
P value for comparison with the non-cirrhosis group, all were statistically significant ($P < 0.05$).

individuals with anxiety/depression problems was the high in the advanced-/terminal-stage HCC (30.7% with moderate to extreme problems) and decompensated cirrhosis (15.4% with moderate to extreme problems) groups.

HSU and EQ-VAS score

The HSU and EQ-VAS scores for the participants are presented in Table 3. The mean HSU of all patients was 0.90 ± 0.18. The HSU for various CHB stages: patients with non-cirrhotic, compensated cirrhosis, decompensated cirrhosis, early-/intermediate-stage HCC and advanced-/terminal-stage HCC, were 0.95 ± 0.08, 0.89 ± 0.16, 0.79 ± 0.19, 0.89 ± 0.12 and 0.52 ± 0.39, respectively. All CHB stages had significantly different HSU values than those in the non-cirrhotic CHB group. The patients in the advanced-/terminal-stage HCC group had the worst HSU.

Likewise, the mean EQ-VAS of all patients was 80.57 ± 14.80. The EQ-VAS for various CHB stages: patients with non-cirrhotic, compensated cirrhosis, decompensated cirrhosis, early-/intermediate-stage HCC and advanced-/terminal-stage HCC were 83.56 ± 12.90, 80.48 ± 13.03, 68.76 ± 17.40, 79.00 ± 14.38 and 62.92 ± 20.62, respectively. All CHB stages had significantly different EQ-VAS compared to that of the non-cirrhotic CHB group. The patients in the advanced-/terminal-stage HCC group had the poorest EQ-VAS.

Correlation and regression coefficient of HSU and EQ-VAS

The HSU and EQ-VAS scores were moderately correlated ($r = 0.469$, $P < 0.001$; Figure 1). We then performed linear regression analyses to predict the change in HSU and EQ-VAS according to the change in the stages of liver disease, adjusted for age, sex and marital status. The results are shown in Tables 4 and 5.

Table 4 presents the regression coefficients and corresponding *P* values for HSU among the different disease stages compared with those in the non-cirrhosis group. As the disease severity increased, the HSU value showed a significant decrease.

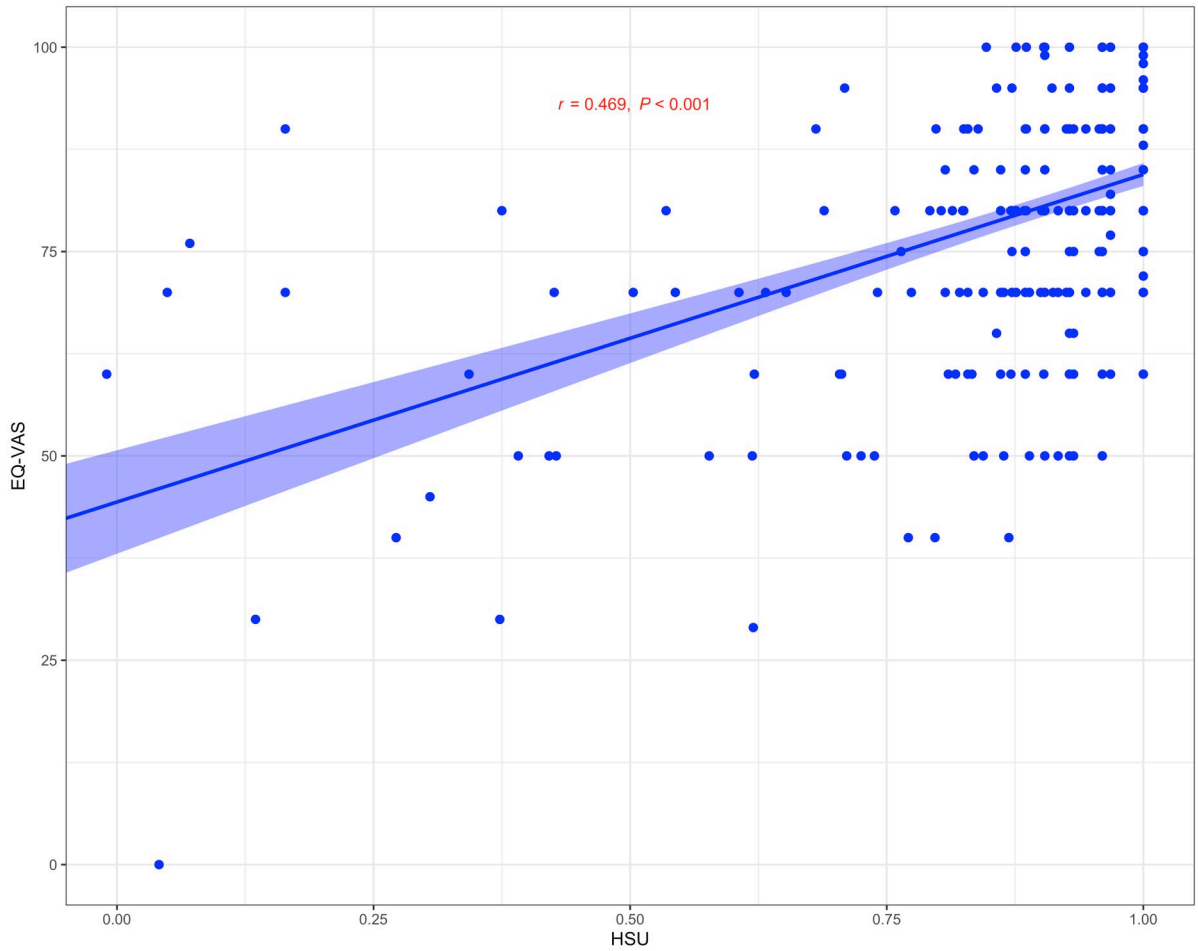

Figure 1. Scatter plot and correlation between HSU and EQ-VAS were reported by the patients in the cohort

Table 4. The regression coefficient of HSU in different disease stages and comparison with the non-cirrhosis group

Group	Regression coefficients	95% CIs	P value
Compensated cirrhosis	−0.048	−0.085, −0.012	0.009
Decompensated cirrhosis	−0.136	−0.219, −0.541	0.001
Early- and intermediate-stage HCC	−0.054	−0.1, −0.009	0.018
Advanced- and terminal-stage HCC	−0.436	−0.497, −0.377	<0.001

The HSU among the CHB stages was adjusted for age (continuous, years), male sex, and marital status (married, single, divorced, and widow/widower).
CIs, confidence intervals; HCC, hepatocellular carcinoma; HSU, health state utility.

Table 5. The regression coefficient of EQ-VAS in different disease stages and comparison with the non-cirrhosis group

Group	Regression coefficients	95% CIs	P value
Compensated cirrhosis	−2.137	−5.632, 1.359	0.230
Decompensated cirrhosis	−13.358	−21.262, −5.456	<0.001
Early- and intermediate-stage HCC	−3.425	−7.777, 0.926	0.122
Advanced- and terminal-stage HCC	−19.957	−25.693, −14.222	<0.001

The EQ-VAS among the CHB stages was adjusted for age (continuous, years), male sex, and marital status (married, single, divorced, and widow/widower).
CIs, confidence intervals; HCC, hepatocellular carcinoma; EQ-VAS, Euroqol-visual analogue scale.

Specifically, compared to the non-cirrhosis group, the regression coefficient for compensated cirrhosis was −0.048 ($P = 0.009$), while the coefficients for decompensated cirrhosis and early-/intermediate-stage HCC were −0.136 ($P = 0.001$) and −0.054 ($P = 0.018$), respectively. The most significant decrease in HSU was observed in the advanced-/terminal-stage HCC group, with a regression coefficient of -0.436 ($P < 0.001$).

Table 5 shows the regression coefficients and *P* values of the EQ-VAS scores for different disease stages compared with those in the non-cirrhosis group. Overall, the same trend of decreasing healthy status perception was observed which is similar to that observed in the HSU findings. However, the significant reduction in EQ-VAS in the different patient groups compared to that in the patients with non-cirrhosis CHB was observed only in the

patients with decompensated cirrhosis and those with advanced-/terminal-stage HCC with regression coefficients of −13.358 ($P < 0.001$) and −19.957 ($P < 0.001$), respectively.

Discussion

To the best of our knowledge, this is the first Thai study that demonstrates HSU in patients with CHB and distinguishes between various stages of CHB. Patients with HCC were divided into two groups: early-/intermediate-stage and advanced-/terminal-stage HCC. In contrast, previous studies only evaluated an entire group of patients with HCC [23, 24].

The key finding of our study revealed that compared to the non-cirrhotic CHB, the HSU values showed a significant decrease with the increase in the disease stages. Similarly, the values of the EQ-VAS scores were lower across the different stages of the disease when compared with those of the non-cirrhosis group. Consequently, the HRQoL, as measured using the HSU values, was in alignment with that perceived by the patients according to the EQ-VAS. Compared to previous studies examining populations from other countries, nearly all stages of CHB in the Thai population had lower HSU and EQ-VAS scores [23, 24]. It was noted that only patients with CHB without cirrhosis or HCC had HSU and EQ-VAS scores that were comparable to those seen in other studies but HSU for other stages is lower. This could be attributed to various factors, such as overall public health facilities, patient perceptions and the general well-being of the population.

We compared the HSU and EQ-VAS to those of healthy Thai people from a previous study. A previous Thai study revealed that the HSU values of individuals without cirrhosis were reminiscent of those of healthy volunteers (non-cirrhosis: 0.95 ± 0.08 *vs* healthy control: 0.93 ± 0.1). In contrast, both the cirrhosis and HCC groups had significantly lower mean HSU values than those of the healthy control group [12]. Similarly, we observed that the patients without cirrhosis exhibited comparable EQ-VAS scores (non-cirrhosis CHB: 83.56 ± 12.90 *vs* healthy control: 83.08 ± 11.88) and the EQ-VAS scores of patients with cirrhosis and HCC were lower than those of healthy volunteers [25].

Our study population comprised respondents with different sociodemographic characteristics, such as employment status, monthly income and educational status. We hypothesized that the disease burden of the patients may affect their employment status and monthly income. Our findings revealed that higher educational levels may have a role in increasing the awareness of the patient regarding CHB treatment and surveillance programs to prevent further disease progression, where patients in the non-cirrhosis group had a higher educational level and were diagnosed with the disease at an early stage.

The EQ-5D-5L descriptive system showed an increasing percentage of individuals with problems in terms of mobility, self-care, usual activities, pain/discomfort and anxiety/depression as the disease progressed. The study also reported a moderate correlation between the HSU and EQ-VAS scores. Even after adjusting for age, sex and marital status, the HSU remained significantly associated with disease severity, which indicates that the EQ-5D-5L is a valid tool for measuring the HRQoL in patients with CHB across different disease stages. Future studies should consider using other HRQoL instruments to corroborate these findings and ensure the generalizability of the results.

Nonetheless, only patients with decompensated cirrhosis and advanced-/terminal-stage HCC showed a discernible decline in the EQ-VAS. Although the regression coefficient values correlated with the progression of the disease, statistical significance was not reached. One plausible interpretation is that while the progression of the disease has a marked effect on preference-based utility values (HSU), the subjective health ratings (EQ-VAS) of the patients might not linearly or prominently align with increasing severity, especially in patients with milder stages, such as compensated cirrhosis and early-/intermediate-stage HCC. Moreover, the EQ-VAS score is a subjective measure that captures an individual's perceived health status at a particular time [26]. In contrast to the HSU, which combines multiple health domains, such as mobility, pain and anxiety, into a single utility score that reflects the preferences of the general population, the EQ-VAS is exclusively based on the perspective of the individual.

The strengths of our study include being the first study in Thailand to investigate HRQoL at various stages of CHB and HCC using both the HSU and EQ-VAS measures. Moreover, this study had a relatively large sample size and included detailed sociodemographic data of the participants. However, this study has some limitations. First, the cross-sectional design posed limitations in establishing causal correlations between disease severity and HRQoL. Secondly, the data in this study were exclusively obtained from a single centre, which may pose limitations on the generalizability of the findings to larger populations. Finally, we eliminated other potential causes from our analysis. Accordingly, future research endeavours should undertake a comparative analysis of many aetiological factors and strive to establish corroborative evidence on larger populations across multiple geographical regions.

Conclusions

Our study demonstrated that the HRQoL of patients with CHB at various stages, from non-cirrhosis to cirrhosis and HCC, as measured using the EQ-5D-5L instrument, decreases with disease progression. This decline in HRQoL was reflected in an increasing percentage of individuals reporting challenges associated with mobility, self-care, usual activities, pain/discomfort and anxiety/depression. The HSU across different stages of CHB in our study would be beneficial for conducting cost-effectiveness and cost-utility analyses studies of similar patients in Thailand. These findings also emphasized the importance of early diagnosis and treatment of CHB to prevent disease progression and improve the HRQoL of the patients. Future longitudinal studies may provide more insights into the causal relationship between disease severity and HRQoL. Furthermore, multicentre studies may help validate and generalize our findings.

Authors' Contributions

R.C., A.K. and P.S. made substantial contributions to the study concept and design, analysis and interpretation of data and drafting of the manuscript. T.P. contributed to data collection and data interpretation. C.K. contributed to the data interpretation. N.C. and P.P are the senior authors responsible for interpreting the data. All authors contributed to the critical revisions and approved the final manuscript.

Funding

This work was supported by the Faculty of Medicine, Prince of Songkla University, Songkhla, Thailand (No.63–368-14–1).

Acknowledgements

We thank Maseetoh Samaeng and Saipin Darawalee for their assistance in this study.

Conflicts of Interest

R. Chantrakul, P. Sripongpun, T. Pattarapuntakul, N. Chamroonkul, C Kongkamol, P. Phisalprapa and A. Kaewdech declare that there is no conflict of interest in this study.

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Gastroenterology Report, 2024, 12, 1–7
https://doi.org/10.1093/gastro/goae015
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