Patient-Reported Outcomes: Does Stigma Affect the Quality of Life of Patients with Chronic Hepatitis B-Related Diseases?

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1. Abstract

1.1. Background & Aim: The degree to which stigma affects the health-related quality of life (HRQoL) of patients with chronic hepatitis B (CHB)-related diseases is not known. We evaluated the HRQoL of patients with CHB-related disease and identified stigma associated with HRQoL.

1.2. Methods: A cross-sectional analysis was performed on data from 576 adult Chinese CHB-related patients from September through December 2019, of whom 387 had CHB, 93 had compensated cirrhosis (CC), 60 had decompensated cirrhosis (DC) and 36 had hepatocellular carcinoma (HCC). The outcomes included the short form 36 health survey version 2 (SF-36v2) scale and Chronic HBV infections-related stigma scale scores.

1.3. Results: The median (25th-75th percentiles) age of study participants was 37 (18-74) years, and 67.9% were male. The median (25th-75th percentiles) PCS score was 52.58 (46.61-56.77), and the median (25th-75th percentiles) MCS score was 42.94 (36.10-51.20). In the multivariate regression analysis, diagnostic typing had a certain effect on the PCS score. Compared to that of the patients with CHB, the PCS of patients with CC, DC or HCC was 3.064 [95% CI: 0.981, 5.148], 5.394 [95% CI: 2.768, 8.020] and 4.497 [95% CI: 0.804, 8.190], respectively. Adding each stigma scale score to the original regression model, the variation in MCS and PCS explained by the model increased from 4.9% to 20.3% and from 22.6% to 23.8%, respectively.

1.4. Conclusion: In China, CHB-related diseases in the CHB stage are mainly manifested in mental HRQoL impairment, and physical HRQoL damage is gradually aggravated with the progression of the disease. Stigma explains some of the substantial variation in HRQoL, especially for mental health.

2. Introduction

World Health Organization (WHO) is promoting the implementation of the global action plan for the eliminate of Hepatitis B virus (HBV). China is the heaviest burden of HBV, and serves as the major contributor to the WHO goal of deaths from viral hepatitis reduced by 65% by 2030 compared to 2015, globally [1,2]. Health-related quality of life (HRQoL) is part of the core data to be collected from patients with chronic hepatitis B (CHB)-related diseases. That

can help us comprehensively understand the patient's experience of CHB-related diseases and provide a basis for action strategies to eliminate hepatitis B.

Stigma against HBV infected persons is a serious problem in the prevention and control of HBV infection. Stigma may be one of the obstacles to eliminating hepatitis B. Previous studies have shown widespread stigma against people with CHB-related diseases in China [3-5]. There have been few studies on the effect of stigma toward patients with CHB-related diseases on HRQoL. Stigma has two meanings. First, stigma refers to the social prejudice, humiliation, and subsequent exclusion and isolation of people who have been stigmatized. Second, the stigmatized person feels as if his or her personal value has diminished and is ashamed of the "stigma." Stigma damages a patients' self-esteem, affects his or her social and economic status, and leads to negative psychology [6]. Whether the stigma of patients with CHB-related diseases will affect the HRQOL of patients has not been studied systematically in China. Questions of how and to what degree specific aspects of stigma affect HRQoL have never been answered.

The purpose of this study was to describe the HRQoL of patients with CHB-related diseases and to investigate the impact of stigma on the HRQoL of these patients. We also examined the relationship between the patients' HRQoL and demographic and clinical characteristics.

3. Material and Methods

3.1. Subjects and Data Collection

A cross-sectional analysis was conducted from September through December 2019 in Zhengzhou city. CHB, Compensated Cirrhosis (CC), Decompensated Cirrhosis (DC) and Hepatocellular Carcinoma (HCC) patients were selected from inpatients and outpatients of the largest provincial tertiary hospital in Zhengzhou, Henan Province. Participant were included in this analysis if they were older than 18 years of age, could express themselves and were diagnosed with a CHB-related disease. Participants were excluded if they had any another chronic disease (e.g., heart disease, hypertension, or diabetes) or coinfection (hepatitis C, hepatitis D or human immunodeficiency virus) (Figure 1). For outpatients, the questionnaires were completed in a quiet office by the patients themselves. For patients who did not understand a survey item, a trained interviewer explained it clearly before the patient provided a response. For inpatients, questionnaires were completed in the ward on the day of admission or the following day in the same way as the outpatients. All protocols were approved by the ethics committee of the hospital, and all participants provided written informed consent.

3.2. Patient-Reported Outcome Measures SF-36v2

Short form 36 health survey version 2 (SF-36v2), which is best suited for a Chinese population, was adopted [7]. The scale includes 36 items with a total of eight scales: Physiological Functioning (PF),

Bodily Pain (BP), Role-Physical (RP), General Health (GH), Vitality (VT), Social Functioning (SF), Role-Emotional (RE) and Mental Health (MH).

3.3. Physical Composite Summary (PCS) and Mental

Composite summary (MCS) were calculated on the basis of 8 scales. PF, RP, BP and GH are closely related to PCS; VT, SF, RE and MH are closely related to MCS. The scale scores range from 0 to 100, with high scores indicating better health. PCS and MCS are based on the standardization of Chinese norms, with a mean of 50 and a standard deviation of 10 [8].

3.4. Chronic HBV Infections-Related Stigma Scale

The Chinese chronic HBV infections-related stigma scale was derived and modified from HIV/AIDS stigma scales; it has good reliability and validity and is applicable to a Chinese population [9]. It consists of 23 items and measures 5 scales: External Discrimination (ED), Negative Self-Evaluation (NSE), Perceived Stigma (PS), Confidentiality (CO) and Secondary Discrimination (SD). Each item was scored using a five-point equidistant score (strongly disagree, disagree, generally, agree and strongly agree). A high score indicates the more serious stigma.

3.5. Sociodemographic and Clinical Covariates

Demographic characteristics of the patients were collected using the general condition questionnaire. Clinical characteristics of the patients were collected for nearly a week and included data on hepatitis B virus surface antigen (HBeAg), Alanine Aminotransferase (ALT), Aspartate Aminotransferase (AST), albumin (ALB), total bilirubin (TBIL), and Alkaline Phosphatase (ALP) levels. Each clinical characteristic was interpreted according to the reference value used in the hospital laboratory.

3.6. Statistical Analyses

Kruskal-Wallis H test was used to compare the scores of each scale. The spearman correlation coefficient was calculated to evaluate the correlation between the scores of all scales and the PCS and MCS scores of the scale and various influencing factors. Unadjusted and adjusted associations between the outcome scores and demographics and clinical characteristics were investigated using multivariable regression models for each scale and the PCS and MCS scores. We first accounted for sociodemographic characteristics (sex and age) and HBV disease stage in the multivariable model and used stepwise regression models for variable selection. The variables in the model that were not significant and contributed little to the interpretation of the dependent variables were deleted. The criterion for entry into the models was with $p<0.05$, and for removal from the models, the criterion was $p>0.1$. Exploratory regression models were conducted to determine whether stigma (total and individual) was an independent predictor of PCS and/or MCS scores, after controlling for the covariates in the initial regression models.

All statistical analyses were performed using SPSS 21.0 statistical

software (IBM Corp., Armonk, NY, USA). All tests were two-sided and p<0.05 was considered statistically significant.

4. Results

4.1. Study Flowchart

According to the clinical diagnosis information, a total of 813 patients with CHB-related diseases were included in this study. According to the exclusion criteria, 152 patients with another chronic disease of coinfection with another disease were excluded. Twenty-four patients refused, and 61 were never found. Finally, a total of 576 SF-36v2 questionnaires and 552 chronic HBV infection-related stigma scales were collected (Figure 1). The effective response rates for the SF-36v2 scale and the chronic HBV infection-related stigma scale were 87.14% and 83.51%, respectively.

4.2. SF-36v2 Results

The average PCS score of the patients with a CHB-related diseases was 50.56, which was similar to the standard of the general population in China (mean of 50), and the average MCS score was 42.84, which was lower than the standard of the general population in China (mean of 50). Results from the pairwise comparison of the four groups are shown in (Table 2). Compared with those of the CHB patients, the PF, RP, BP, GH, VT, RE and PCS scores of the CC DC and HCC patients were lower. Compared with those of the CC patients, the RP, BP, GH, RE and PCS scores of the DC patients

were lower. The PF, RP, BP, GH, VT, SF and PCS scores of the HCC patients were lower. There was no significant difference in the scores of the DC patients and HCC patients for any scale (Table 1).

4.3. Chronic HBV Infection-Related Stigma Scale Score Results

Differences were analyzed on all scales of the stigma scale for the four groups; the ED and CO scores of HCC patients were significantly different from those of CHB patients, and the NSE scores of the HCC patients were significantly different from those of the DC patients (Table A2).

4.4. Bivariate Associations Between SF-36v2 Scores and Covariates

The correlation between the PCS score and scales of the stigma scale scores was weak. The correlation between the MCS score and NSE scale score of the stigma scale was the strongest (r =-0.369), while the correlation between the MCS score and ED scale score (r =-0.269), and the PH scale score (r=-0.301) and SD scale score (r =-0.246) was weak. Among the eight scales, the correlation between the RP, SF and RE scores and the NSE score was the strongest, while the correlation between the scores of the other scales and the scores of the stigma scale was weak (r =-0.3~0.1) (Figure A1). The results of the spearman correlation analysis of the SF-36v2 scale scores and sociodemographic and clinical covariates are shown in (Figure A2).
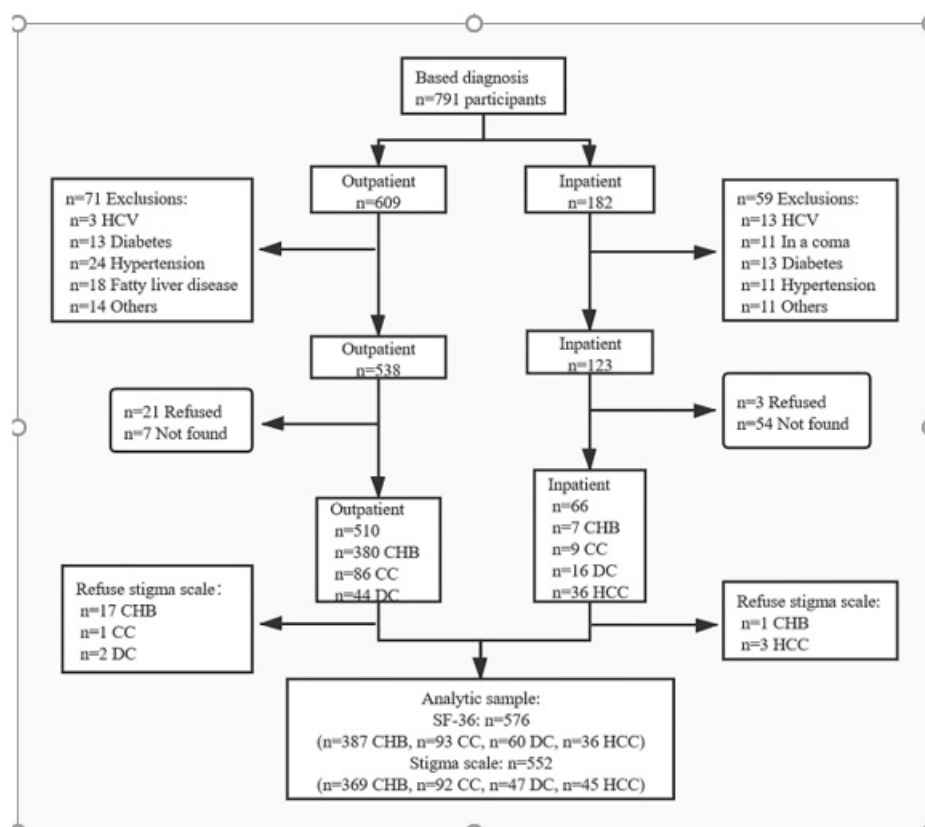

Figure 1: Study flow chart

Appendix

	ED	NSE	PS	CC	SD
PF	-0.102	-0.144	-0.121	0.022	-0.076
RP	-0.289	-0.363	-0.283	-0.071	-0.223
BP	-0.087	-0.18	-0.138	0.02	-0.058
GH	-0.143	-0.175	-0.144	0.063	-0.103
VT	-0.162	-0.151	-0.165	-0.02	-0.1
SF	-0.219	-0.356	-0.268	-0.098	-0.18
RE	-0.241	-0.348	-0.24	-0.115	-0.209
MH	-0.264	-0.245	-0.216	0.01	-0.172
PCS	-0.201	-0.219	-0.185	0.006	-0.094
MCS	-0.269	-0.369	-0.301	-0.083	-0.246

Spearman Corr: -1.0, -0.5, 0.0, 0.5, 1.0

Figure A1: Spearman correlations for bivariate associations of SF-36 v2 Physical Composite Summary Score(PCS), SF-36 v2 Mental Composite Summary Score(MCS) and chronic HBV-infections related stigma Scales. Non-significant (p<0.05) correlation coefficients are labeled with " " .

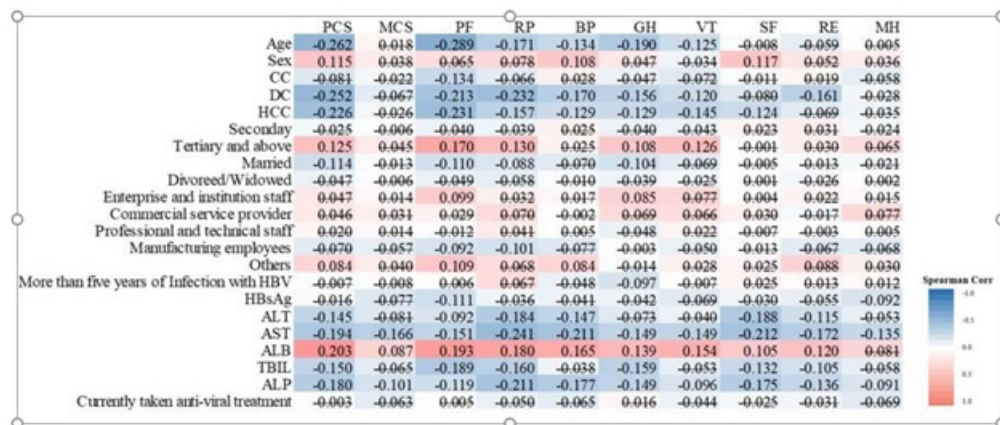|	PCS	MCS	PF	RP	BP	GH	VT	SF	RE	MH
Age	-0.262	0.018	-0.289	-0.171	-0.134	-0.190	-0.125	-0.008	-0.059	0.005
Sex	0.115	0.038	0.065	0.078	0.108	0.047	-0.034	0.117	0.052	0.036
CC	-0.081	-0.022	-0.134	-0.066	0.028	-0.047	-0.072	-0.011	0.019	-0.058
DC	-0.252	-0.067	-0.213	-0.232	-0.170	-0.156	-0.120	-0.080	-0.161	-0.028
HCC	-0.226	-0.026	-0.231	-0.157	-0.129	-0.129	-0.145	-0.069	-0.069	-0.035
Secondary	-0.025	-0.006	-0.040	-0.039	0.025	-0.040	-0.043	0.023	0.031	-0.024
Tertiary and above	0.125	0.045	0.170	0.130	0.025	0.108	0.126	-0.001	0.030	0.065
Married	-0.114	-0.013	-0.110	-0.088	-0.070	-0.104	-0.069	-0.005	-0.013	-0.021
Divoreed/Widowed	-0.047	-0.006	-0.049	-0.058	-0.010	-0.039	-0.025	0.001	-0.026	0.002
Enterprise and institution staff	0.047	0.014	0.099	0.032	0.017	0.085	0.077	0.004	0.022	0.015
Commercial service provider	0.046	0.031	0.029	0.070	-0.002	0.069	0.066	0.030	-0.017	0.077
Professional and technical staff	0.020	0.014	-0.012	0.041	0.005	-0.048	0.022	-0.007	-0.003	0.005
Manufacturing employees	-0.070	-0.057	-0.092	-0.101	-0.077	-0.003	-0.050	-0.013	-0.067	-0.068
Others	0.084	0.040	0.109	0.068	0.084	-0.014	0.028	0.025	0.088	0.030
More than five years of Infection with HBV	-0.007	-0.008	0.006	0.067	-0.048	-0.097	-0.007	0.025	0.013	0.012
HBsAg	-0.016	-0.077	-0.111	-0.036	-0.041	-0.042	-0.069	-0.030	-0.055	-0.092
ALT	-0.145	-0.081	-0.092	-0.184	-0.147	-0.073	-0.040	-0.188	-0.115	-0.053
AST	-0.194	-0.166	-0.151	-0.241	-0.211	-0.149	-0.149	-0.212	-0.172	-0.135
ALB	0.203	0.087	0.193	0.180	0.165	0.139	0.154	0.105	0.120	0.081
TBIL	-0.150	-0.065	-0.189	-0.160	-0.038	-0.159	-0.053	-0.132	-0.105	-0.058
ALP	-0.180	-0.101	-0.119	-0.211	-0.177	-0.149	-0.096	-0.175	-0.136	-0.091
Currently taken anti-viral treatment	-0.003	-0.063	0.005	-0.050	-0.065	0.016	-0.044	-0.025	-0.031	-0.069

Spearman Corr

Figure A2: Spearman correlations for bivariate associations of SF-36 v2 Physical Composite Summary Score(PCS), SF-36 v2 Mental Composite Summary Score(MCS) and characteristics, clinical Characteristics. Non-significant (p<0.05) correlation coefficients are labeled with " " .

Table 1: Demographic of participants

Characteristics	CHB (n=387)	CC (n=93)	DC (n=60)	HCC (n=36)
Age n(%)				
Median(25th-75th percentiles)	34.0(30.0-41.0)	41.38(34.5-48.0)	45.77(36.5-54.0)	53.86(48.3-63.5)
Min-Max	18.0-63.0	22.0-62.0	24.0-74.0	23.0-72.0
Sex n(%)				
Male	239(61.8)	75(80.6)	48(80.0)	29(80.6)
Female	148(38.2)	18(19.4)	12(20.0)	7(19.4)
Marital status n(%)				
Single	48(12.4)	5(5.4)	5(8.3)	0(0)
Married	334(86.3)	87(93.5)	51(85.0)	35(97.2)
Divorced/Widowed	5(1.3)	1(1.1)	4(6.7)	1(2.8)
Education level n(%)				
Primary and under	24(6.2)	15(16.2)	13(21.6)	13(36.2)
Secondary	174(45.0)	54(58.1)	33(45.0)	21(58.3)

Tertiary and above	189(48.8)	24(25.8)	14(23.4)	2(5.6)
Occupation n(%)				
Farmer	26(6.7)	17(18.3)	12(20.0)	16(44.4)
Enterprise and institution staff	94(24.2)	21(22.6)	9(15.0)	3(8.3)
Commercial service provider	39(10.1)	4(4.3)	4(6.7)	0(0)
Professional and technical staff	41(15.8)	6(6.5)	4(6.7)	1(2.8)
Manufacturing employees	61(15.8)	20(21.5)	19(31.7)	8(22.2)
Others	126(32.6)	25(26.9)	12(20.0)	8(22.2)

Abbreviations: CHB, chronic hepatitis B; CC, compensated cirrhosis; DC, decompensated cirrhosis: HCC, hepatocellular carcinoma;
Min-Max: minimum and maximum

Table 2: Median SF-36v2 Scores (25th -75th Percentiles) for Each Group of Patients

SF-36v2	CHB (n=387)	CC (n=93)	DC (n=60)	HCC (n=36)
PF	93.68(95.00~100.00)	84.14(77.50~100.00)*	81.67(75.00~95.00)*	75.28(55.00~93.75)*, **
RP	85.84(75.00~100.00)	76.55(56.25~100.00)*	60.28(25.00~87.50)*, **	63.89(37.50~93.75)*, **
BP	85.15(74.00~100.00)	81.84(68.00~100.00)	70.68(52.00~96.00)*, **	67.72(43.50~100.00)*, **
GH	56.70(45.00~72.00)	50.61(37.50~62.00)*	42.70(25.50~57.00)*, * *	42.19(27.75~56.50)*, **
VT	63.31(50.00~75.00)	56.31(50.00~68.75)*	52.50(43.75~68.75)*	50.00(37.50~56.25)*, **
SF	83.91(75.00~100.00)	80.91(62.50~100.00)	76.25(62.50~100.00)*	75.00(50.00~100.00)*, **
RE	81.80(75.00~100.00)	79.66(66.67~100.00)	68.75(50.00~91.67)*, **	67.71(50.00~100.00)*
MH	69.43(55.00~80.00)	65.75(50.00~80.00)	66.58(55.00~83.75)	71.99(52.08~100.00)
PCS	54.01(49.55~57.78)	52.26(43.39~55.49)*	44.05(37.22~52.54)*, **	41.04(34.86~50.97)*, **
MCS	44.16(36.76~51.92)	42.33(35.00~50.96)	40.17(34.30~49.34)	41.77(38.09~50.15)

Abbreviations: PF, physical functioning: RP, role physical: BP, bodily pain: GH, general health, VT, vitality: SF, social functioning:
RE, role emotional: MH, mental health; PCS, physical component summary: MCS, mental component summary; CHB: chronic
hepatitis B; CC: compensated cirrhosis; DC: decompensated cirrhosis: HCC: hepatocellular carcinoma.
*p<0.05compared with patients with CHB; **P<0.05 compared with patients with CC.

Table A1: Clinical Characteristics of participants

	CHB n=387	CC n=93	DC n=60	HCC n=36
Duration of Infection with HBV n (%)				
More than five years	302(78.0)	66(71.0)	44(73.3)	25(69.4)
Less than five years	85(22.0)	27(29.0)	16(26.7)	11(30.6)
Currently taken anti-viral treatment n (%)				
Yes	313(80.9)	85(91.4)	52(86.7)	27(75.0)
No	74(19.1)	8(8.6)	8(13.3)	9(25.0)
	n=360	n=73	n=47	n=8
Quantitative HBsAg (log10 IU/mL)				
Median (IQR)	3.38(3.00,4.10)	3.20(2.80,3.72)	2.57(1.96,3.43)	2.34(1.62~3.17)
Min-Max	<LLOD~5.10	0.91~4.34	<LLOD~4.50	1.32~3.35
	n=356	n=73	n=55	n=33
ALT(U/L)				
Median (IQR)	50.13(18.60-47.25)	37.09(20.85-47.40)	47.83(25.30-48.70)	64.94(21.70-59.90)
Min-Max	5.20-1920.00	10.50-167.80	15.10-360.90	12.10-512.60
AST(U/L)				
Median (IQR)	40.16(20.80-35.38)	31.20(22.45-33.85)	47.12(26.70-55.30)	79.88(28.85-89.00)
Min-Max	10.40-1477.00	17.10-109.20	18.20-243.70	14.10-445.10
ALB (g/L)				
Median (IQR)	46.82(44.80-48.90)	46.76(45.35-48.45)	40.60(34.30-47.60)	35.19(30.65-40.45)
Min-Max	28.50-55.50	33.00-55.40	22.10-51.00	21.90-46.30
TBIL (mmol/L)				
Median (IQR)	12.04(7.63-14.30)	13.98(8.35-16.70)	31.21(10.30-26.50)	28.65(30.65-40.45)
Min-Max	2.80-102.40	4.70-55.00	3.70-321.60	6.60-248.70
ALP (U/L)				
Median (IQR)	75.58(60.00-87.75)	77.08(57.50-90.00)	107.33(69.00-109.00)	152.73(76.00-185.00)
Min-Max	8.00-255.00	3.70-164.00	47.00-352.00	39.00-819.00

CHB, chronic hepatitis B; CC, compensated cirrhosis; DC, decompensated cirrhosis: HCC, hepatocellular carcinoma; ALT, alanine
aminotransferase; AST, aspartate aminotransferase; TBIL, total bilirubin; ALB, albumin; ALP, alkaline phosphatase; IQR, interquartile range; Min-
Max: minimum and maximum; LLOD: Lower limit of detection (Quantitative HBsAg: 0.05 IU/mL=-1.3log10 IU/mL).

Table A2: Median chronic HBV-infections related stigma scale Scores (25th -75th Percentiles) for Each Group of Patients

Scale	CHB(n=369)	CC (n=92)	DC(n=58)	HCC(n=33)	Overall(n=552)
ED	13(10~16)	12.50(8.25~15)	14(10~15.25)	11(8.50~14)*	13(10~16)
NSE	11(8~14)	12(8.25~15.00)	12(8.75~15)	9(7~13)‡	11(8~14)
PS	21(15~24)	21(14~24)	21(15~26.25)	20(9~24)	21(14.25~24)
CO	15(12~16)	14(11~16)	12(12~17)	14(11~16)*	14(12~16)
SD	7(6~9)	8(6~9)	7(6~9)	6(3~9)	7(6~9)
Abbreviations: ES, external discrimination: NSE, negative self-evaluation: PS, perceived stigma: CO, confidentiality; SD, secondary discrimination; CHB: chronic hepatitis B; CC: compensated cirrhosis; DC: decompensated cirrhosis: HCC: hepatocellular carcinoma. *p<0.05compared with patients with CHB; †P<0.05 compared with patients with CC; ‡p<0.05 compared with patients with DC.					

4.5. Unadjusted and Adjusted Associations Between SF-36v2 Scores and Sociodemographic and Clinical Covariates

Unadjusted associations between each scale and the PCS and MCS scores, demographics data and clinical covariates are provided in (Table A3). When the PCS score was the dependent variable, it was significant and contributed significantly to the variation in the dependent variable: age, gender, ALT AST, ALB, TBIL, ALP, diagnostic typing or marital status (9 factors). When the MCS score was the dependent variable, the significant independent variables included HBsAg, TBIL and ALP level obtained the year of hepatitis B diagnosis.

For the multivariable analyses, we first considered demographic indicators (gender and age) and then used a stepwise regression approach to select sociodemographic and clinical characteristic variables. In the regression model based on the PCS and MCS score as the dependent variables, the explanatory variations of the independent variables to dependent variables were 24.0% and 4.2%, respectively.

The model with the PCS score as the dependent variable showed that PCS scores of the CC patients with DC and the HCC patients were reduced by 3.064 [95% CI: 0.981, 5.148], 5.394 [95% CI: 2.768, 8.020] and 4.497 [95% CI: 0.804, 8.190] points. PCS scores were reduced by 0.767 [95%CI: 0.021, 1.513] points for every 10 years of age. The PCS scores were negatively correlated with ALB and ALP level anomalies. For the model with the MCS score as the dependent variable, compared with those of the CHB patients, the MCS scores of the DC patients decreased by 3.655 [95% CI: 0.165, 7.144] points. MCS scores were reduced by 1.137 [95% CI: 0.082, 2.192] points for every 10 years of age. Abnormal ALP was associated with a lower MCS score (Table 3). In the regression model based on the PF, RP, BP, GH, VT, SF, RE and MH scale scores as the dependent variables, the explanatory variations of the independent variables to dependent variables were 18.0%, 17.2%, 15.0%, 10.7%, 9.7%, 13.4%, 6.7% and 3.6%, respectively (Table A4).

Table 3: Adjusted associations between SF-36 v2 scores with CHB-related characteristics andclinical indicators (n =574)

Predictors	PCS Mean difference(95% CI)	p	MCS Mean difference(95% CI)	p
Age, per 10 years	-0.767(-1.513, -0.021)	0.044	1.137(0.082, 2.192)	0.035
Sex				
Male	Reference		Reference	
Female	1.231(-0.279, 2.740)	0.110	-0.486(-2.606, 1.634)	0.653
HBV disease stage				
CHB	Reference		Reference	
CC	-3.064(-5.148, -0.981)	0.004	-1.319(-4.285, 1.646)	0.382
DC	-5.394(-8.020, -2.768)	<0.001	-3.655(-7.144,-0.165)	0.040
HCC	-4.497(-8.190, -0.804)	0.017	-2.526(-7.278,2.225)	0.297
ALB	0.338(0.163, 0.513)	<0.001		
ALP	-0.021(-0.037, -0.006)	0.006	-0.036(-0.057,-0.016)	0.001
Model R²	R²=0.240		R²=0.042	
Abbreviations: PCS: Physical component summary; MCS: Mental component summary; CHB: chronic hepatitis B; CC: compensated cirrhosis; DC: decompensated cirrhosis: HCC: hepatocellular carcinoma; ALB, albumin; ALP: alkaline phosphatase.				

Table A3: Unadjusted associations between SF-36 v2 scores with CHB-related characteristics and clinical Characteristics (n=574)

Predictors	PF Mean difference (95% CI)	RP Mean difference (95% CI)	BP Mean difference (95% CI)	GH Mean difference (95% CI)	VT Mean difference (95% CI)	SF Mean difference (95% CI)	RE Mean difference (95% CI)	MH Mean difference (95% CI)	PCS Mean difference (95% CI)	MCS Mean difference (95% CI)
Age, per 10 years	-4.381 (-5.562, -3.201) R²=0.085	-3.895 (-5.814, -1.976) R²=0.027	-2.981 (-4.571, -1.391) R²=0.023	-3.512 (-5.071, -1.953) R²=0.033	-2.682 (-4.185, -1.179) R²=0.021	-1.074 (-2.612, 0.465) R²=0.003	-0.623 (-2.433, 1.186) R²=0.001	-0.220 (-1.609, 1.168) R²=0.000	-2.576 (-3.251, -1.900) R²=0.089	0.366 (-0.532, 1.264) R²=0.001
Sex										
Male	Reference	Reference	Reference	Reference	Reference	Reference	Reference	Reference	Reference	Reference

Predictors	PF	RP	BP	GH	VT	SF	RE	MH	PCS	MCS
Female	1.737 (-1.075, 4.550) R^2=0.003	5.829 (1.413, 10.245) R^2=0.012	5.015 (1.359, 8.671) R^2=0.013	2.578 (-1.035, 6.191) R^2=0.003	-1.329 (-4.794, 2.137) R^2=0.001	4.967 (1.467, 8.468) R^2=0.013	3.347 (-0.777, 7.470) R^2=0.004	1.163 (-2.005, 4.320) R^2=0.001	2.116 (0.506, 3.725) R^2=0.012	0.678 (-1.376, 2.732) R^2=0.001
HBV disease stage										
CHB	Reference	Reference	Reference	Reference	Reference	Reference	Reference	Reference	Reference	Reference
CC	-9.542 (-12.933, -6.151)	-9.291 (-14.670, -3.912)	-3.312 (-7.892, 1.269)	-6.087 (-10.620, -1.554)	-6.990 (-11.342, -2.639)	-2.991 (-7.446, 1.463)	-2.145 (-7.409, 3.119)	-3.679 (-7.768, 0.410)	-4.453 (-6.345, -2.560)	-0.884 (-3.534, 1.766)
DC	-12.016 (-16.090, -7.941)	-25.561 (-32.071, -19.051)	-14.467 (-19.969, -8.965)	-14.003 (-19.449, -8.556)	-10.807 (-16.035, -5.580)	-7.655 (-13.006, -2.305)	-13.054 (-19.379, -6.730)	2.848 (-7.761, 2.065)	-9.792 (-12.082, -7.502)	-2.389 (-5.596, 0.818)
HCC	-18.404 (-23.521, -13.288) R^2=0.137	-21.948 (-30.064, -13.832) R^2=0.127	-17.428 (-24.338, -10.518) R^2=0.075	-14.506 (-21.345, -7.666) R^2=0.067	-15.391 (-21.956, -8.825) R^2=0.063	-16.197 (-22.917, -9.478) R^2=0.047	-9.814 (17.756, -1.871) R^2=0.035	-4.848 (-11.018, 1.322) R^2=0.009	-11.664 (-14.519, -8.809) R^2=0.184	-2.612 (-6.609, 1.386) R^2=0.006
Marital status										
Single	Reference	Reference	Reference	Reference	Reference	Reference	Reference	Reference	Reference	Reference
Married	-6.402 (-10.743, -2.062)	-8.055 (-14.908, -1.203)	-4.407 (-10.105, 1.291)	-8.571 (-14.149, -2.994)	-5.880 (-11.249, -0.0080.512)	-1.527 (-6.995, 3.942)	-0.619 (-7.039, 5.800)	-1.280 (-6.206, 3.646)	-4.420 (-6.901, -1.939)	0.152 (-3.035, 3.340)
Divorced/Widowed	-11.967 (-22.266, -1.669) R^2=0.017	-20.778 (-37.034, -4.522) R^2=0.015	-5.636 (-19.154, 7.881) R^2=0.004	-14.445 (-27.677, -1.213) R^2=0.018	-7.455 (-20.191, 5.281) R^2=0.008	-1.156 (-14.128, 11.816) R^2=0.001	-7.455 (-22.675, 7.785) R^2=0.002	-1.669 (-13.357, 10.018) R^2=0.000	-7.980 (-13.865, -2.096) R^2=0.024	-0.092 (-7.653, 7.469) R^2=0.000
Education level										
Primary and below	Reference	Reference	Reference	Reference	Reference	Reference	Reference	Reference	Reference	Reference
Secondary	7.824 (3.581, 12.066)	8.797 (2.046, 15.548)	4.479 (-1.169, 10.127)	5.124 (-0.410, 10.658)	5.522 (0.230, 10.813)	3.478 (-1.944, 8.900)	6.404 (0.053, 12.756)	2.304 (-2.574, 7.182)	3.819 (1.375, 6.263)	1.477 (-1.686, 4.639)
Tertiary and over	11.574 (7.241, 15.908) R^2=0.047	14.195 (7.302, 21.088) R^2=0.030	6.089 (0.322, 11.856) R^2=0.008	8.893 (3.240, 14.546) R^2=0.018	9.392 (3.987, 14.797) R^2=0.022	3.635 (-1.902, 9.171) R^2=0.003	6.942 (0.454, 13.429) R^2=0.008	4.145 (-0.837, 9.128) R^2=0.005	6.015 (3.520, 8.510) R^2=0.040	1.811 (-1.417, 5.038) R^2=0.002
Occupation										
Farmer	Reference	Reference	Reference	Reference	Reference	Reference	Reference	Reference	Reference	Reference
Enterprise and institution staff	9.974 (5.391, 17.213)	12.810 (5.541, 20.079)	6.298 (0.228, 12.367)	10.644 (4.699, 16.589)	12.171 (6.503, 17.840)	6.973 (1.149, 12.796)	6.844 (0.008, 13.681)	3.892 (-1.356, 9.139)	5.839 (3.205, 8.437)	2.665 (-0.744, 6.073)
Commercial service provider	11.398 (5.583, 17.213)	15.742 (6.531, 24.953)	6.759 (-0.943, 14.461)	12.618 (5.074, 20.162)	13.127 (5.934, 20.321)	8.338 (0.948, 15.728)	4.485 (-4.191, 13.161)	7.803 (1.144, 14.462)	6.580 (3.243, 9.918)	3.404 (-0.915, 7.723)

Table A3: Unadjusted associations between SF-36 v2 scores with CHB-related characteristics and clinical indicators (n=574)

Predictors	PF Mean difference (95% CI)	RP Mean difference (95% CI)	BP Mean difference (95% CI)	GH Mean difference (95% CI)	VT Mean difference (95% CI)	SF Mean difference (95% CI)	RE Mean difference (95% CI)	MH Mean difference (95% CI)	PCS Mean difference (95% CI)	MCS Mean difference (95% CI)
Professional and technical staff	8.080 (2.435, 13.744)	14.745 (5.804, 23.686)	5.726 (-1.750, 13.201)	4.508 (-2.815, 11.830)	10.570 (3.587, 17.553)	6.027 (-1.147, 13.200)	6.548 (-1.873, 14.969)	2.891 (-3.572, 9.355)	5.105 (1.866, 8.345)	2.129 (-2.063, 6.322)
Others	9.554 (5.188, 13.920) R^2=0.047	13.484 (6.568, 20.400) R^2=0.037	7.420 (1.632, 13.207) R^2=0.016	7.370 (1.706, 13.034) R^2=0.028	10.106 (4.705, 15.507) R^2=0.037	6.796 (1.243, 12.349) R^2=0.013	8.249 (1.735, 14.763) R^2=0.014	3.549 (-1.451, 6.194) R^2=0.013	5.535 (3.027, 8.043) R^2=0.045	2.656 (-0.590, 5.902) R^2=0.007
Duration of illness										
Less than five years	Reference	Reference	Reference	Reference	Reference	Reference	Reference	Reference	Reference	Reference

Predictor	PF	RP	BP	GH	VT	SF	RE	MH	PCS	MCS
More than five years	2.407 (-0.660, 5.074)	3.955 (-0.880, 8.790)	-1.402 (-5.419, 2.614)	-4.619 (-8.550, -0.687)	-0.330 (-4.114, 3.453)	1.068 (-2.780, 4.916)	0.064 (-4.446, 4.574)	-0.047 (-3.505, 3.412)	0.676 (-1.091, 2.444)	-0.677 (-2.920, 1.566)
	R^2=0.004	R^2=0.004	R^2=0.001	R^2=0.009	R^2=0.000	R^2=0.001	R^2=0.000	R^2=0.000	R^2=0.001	R^2=0.001
Currently taken anti-viral treatment										
No	Reference	Reference	Reference	Reference	Reference	Reference	Reference	Reference	Reference	Reference
Yes	1.637 (-1.846, 5.120)	-2.857 (-8.348, 2.634)	-3.888 (-8.423, 0.647)	-0.112 (-4.519, 4.368)	-2.833 (-7.117, 1.452)	-1.168 (-5.522, 3.185)	1.598 (-6.711, 3.515)	-2.555 (-6.472, 1.362)	-0.144 (-2.144, 1.856)	-1.661 (-4.195, 0.874)
	R^2=0.001	R^2=0.002	R^2=0.005	R^2=0.000	R^2=0.003	R^2=0.000	R^2=0.001	R^2=0.003	R^2=0.000	R^2=0.003
HBsAg	-9.045 (-20.463, 2.373)	-4.192 (-23.204, 14.820)	-7.747 (-23.277, 7.784)	-9.066 (-25.551, 7.419)	-12.239 (-27.665, 3.186)	-6.816 (-21.550, 7.918)	-9.853 (-27.992, 8.285)	-14.122 (-28.313, 0.069)	-2.063 (-8.816, 4.690)	-7.841 (-17.012, 1.330)
	R^2=0.005	R^2=0.000	R^2=0.002	R^2=0.002	R^2=0.005	R^2=0.002	R^2=0.002	R^2=0.008	R^2=0.000	R^2=0.006
ALT	0.001 (-0.013, 0.014)	-0.030 (-0.0.51, -0.009)	-0.004 (-0.022, 0.013)	-0.009 (-0.026, 0.009)	-0.008 (-0.025, 0.008)	-0.013 (-0.030, 0.003)	0.000 (-0.020, 0.019)	0.001 (-0.014, 0.016)	-0.007 (-0.015, 0.000)	0.000 [-0.010, 0.010]
	R^2=0.000	R^2=0.015	R^2=0.000	R^2=0.002	R2=0.002	R^2=0.005	R^2=0.977	R^2=0.000	R^2=0.007	R^2=0.000
AST	-0.008 (-0.025, 0.010)	-0.054 (-0.082, -0.027)	-0.016 (-0.040, 0.007)	-0.020 (-0.043, 0.003)	-0.026 (-0.048, -0.004)	-0.032 (-0.053, -0.010)	-0.014 (-0.040, 0.012)	-0.009 (-0.029, 0.011)	-0.014 (-0.025, -0.004)	-0.007 (-0.020, 0.005)
	R^2=0.001	R^2=0.028	R^2=0.004	R^2=0.006	R^2=0.010	R^2=0.015	R^2=0.002	R^2=0.001	R^2=0.013	R^2=0.002
ALB	0.200 (0.100, 0.300)	0.271 (0.112, 0.429)	0.184 (0.053, 0.315)	0.071 (-0.059, 0.201)	0.080 (-0.044, 0.205)	0.225 (0.101, 0.350)	0.209 (0.062, 0.356)	0.061 (-0.053, 0.174)	0.068 (0.017, 0.119)	0.025 (-0.040, 0.090)
	R^2=0.027	R^2=0.020	R^2=0.013	R^2=0.002	R^2=0.003	R^2=0.022	R^2=0.014	R^2=0.002	R^2=0.012	R^2=0.001
TBIL	-0.106 (-0.165, -0.048)	-0.201 (-0.293, -0.110)	-0.163 (-0.239, -0.086)	-0.145 (-0.221, -0.069)	-0.095 (-0.169, -0.021)	-0.134 (-0.206, -0.062)	-0.127 (-0.214, -0.041)	-0.109 (-0.176, -0.043)	-0.076 (-0.109, -0.042)	-0.058 (-0.101, -0.015)
	R^2=0.024	R^2=0.035	R^2=0.032	R^2=0.026	R^2=0.012	R^2=0.025	R^2=0.016	R^2=0.020	R^2=0.037	R^2=0.014
ALP	-0.075 (-0.100, -0.049)	-0.129 (-0.169, -0.090)	-0.108 (-0.141, -0.075)	-0.080 (-0114, -0.047)	-0.068 (-0.101, -0.036)	-0.123 (-0.153, -0.092)	-0.089 (-0.126, -0.051)	-0.059 (-0.088, -0.029)	-0.053 (-0.067, -0.039)	-0.038 (0.057, -0.019)
	R^2=0.061	R^2=0.074	R^2=0.074	R^2=0.041	R^2=0.032	R^2=0.108	R^2=0.040	R^2=0.029	R^2=0.093	R^2=0.029

Abbreviations: PF, physical functioning: RP, role physical: BP, bodily pain: GH, general health, VT, vitality: SF, social functioning: RE, role emotional: MH, mental health; PCS: Physical component summary; MCS: Mental component summary; CHB, chronic hepatitis B; CC, compensated cirrhosis; DC, decompensated cirrhosis: HCC, hepatocellular carcinoma; ALT, alanine aminotransferase; AST, aspartate aminotransferase; TBIL, total bilirubin; ALB, albumin; ALP, alkaline phosphatase.

Table A4: Adjusted associations between SF-36 v2 scores with CHB-related characteristics and clinical indicators (n =574)

Predictors	PF Mean difference (95% CI)	RP Mean difference (95% CI)	BP Mean difference (95% CI)	GH Mean difference (95% CI)	VT Mean difference (95% CI)	SF Mean difference (95% CI)	RE Mean difference (95% CI)	MH Mean difference (95% CI)
Age, per 10 years	-1.740 (-3.090, -0.390) P=0.012	0.558 (-1.572, 2.689) P=0.607	0.003 (-1.804, 1.809) P=0.998	-0.162 (-0.356, 0.031) P=0.100	-0.364 (-2.122, 1.394) P=0.684	1.560 (-0.136, 3.256) P=0.071	1.835 (-0.258, 3.928) P=0.086	0.787 (-0.859, 2.433) P=0.348
Sex								
Male	Reference	Reference	Reference	Reference	Reference	Reference	Reference	Reference
Female	0.008 (-2.720, 2.735) P=0.996	3.182 (-1.130, 7.494) P=0.148	4.442 (0.786, 8.098) P=0.017	-0.280 (-3.940, 3.380) P=0.881	-4.556 (-8.082, -1.030) P=0.011	2.772 (-0.635, 6.179) P=0.111	1.064 (-3.134, 5.262) P=0.619	-0.574 (-3.875, 2.727) P=0.733
HBV disease stage								
CHB	Reference	Reference	Reference	Reference	Reference	Reference	Reference	Reference
CC	-7.572 (-11.343, -3.801) P<0.001	-6.574 (-12.534, -0.614) P=0.031	-0.330 (-5.377, 4.717) P=0.898	-5.455 (-10.604, -0.306) P=0.038	-8.261 (-13.202, -3.320) P=0.001	-2.885 (-7.622, 1.912) P=0.240	-0.763 (-6.645, 5.120) P=0.799	-3.524 (-8.150, 1.102) P=0.135
DC	-5.639 (-10.338, -0.939) P=0.019	-17.605 (-25.123, -10.087) P<0.001	-7.408 (-13.698, -1.119) P=0.021	-11.277 (-17.33., -5.223) P<0.001	-11.875 (-17.645, -6.104) P<0.001	-6.268 (-11.835, -0.702) P=0.027	-12.467 (-19.336, -5.597) P<0.001	-3.831 (-9.233, 1.571) P=0.164

HCC	-6.096 (-12.770, 0.579) P=0.073	-9.487 (-20.038, 1.064) P=0.078	-3.770 (-12.702, 5.162) P=0.407	-9.419 (-17.753, -1.084) P=0.027	-12.645(-20.562, -4.727) P=0.002	-11.621 (-19.259, -3.983) P=0.003	-7.567 (-16.993, 1.858) P=0.115	-2.923 (-10.335, 4.488) P=0.439
AST		-0.032 (-0.059, -0.005) P=0.019						
ALB	0.524 (0.208, 0.840) P=0.001	0.612 (0.117, 1.126) P=0.016	0.849 (0.427, 1.272) P<0.001					
ALP	-0.031 (-0.058, -0.003) P=0.028	-0.060 (-0.103, -0.016) P=0.008	-0.051 (-0.088, -0.015) P=0.006	-0.050 (-9.178, -1.183) P=0.006	-0.043 (-0.077, -0.009) P=0.013	-0.103 (-0.136, -0.070) P<0.001	-0.073 (-0.113, -0.032) P=0.001	-0.056 (-0.088, -0.024) P=0.001
Model R²	R²=0.180	R²=0.172	R²=0.150	R²=0.107	R²=0.097	R²=0.134	R²=0.067	R²=0.036

Abbreviations: PF, physical functioning: RP, role physical: BP, bodily pain: GH, general health, VT, vitality: SF, social functioning: RE, role emotional: MH, mental health; CHB: chronic hepatitis B; CC: compensated cirrhosis; DC: decompensated cirrhosis: HCC: hepatocellular carcinoma; AST, aspartate aminotransferase; ALB, albumin; ALP: alkaline phosphatase.

4.6. Exploratory Analyses of Stigma Predicting SF-36v2 Scales

On the basis of the regression model in which the scores of each scale are dependent variables, the scores of each scale in the stigma scale are entered into the model as independent variables. The results show that for the stigma of the scale scores on the basis of the original model, the predictive power of the PCS and MCS scores range from 22.6% to 23.8% and from 4.9% to 20.3%, respectively. The predictive power of the PF, RP, BP, GH, VT, RP, and RE scores from 16.6% to 19.2%, from 15.9% to 18.4%, from 14.5% to 16.5%, from 8.6% to 21.6%, from 13.3% to 19.4%, from 7.6% to 14.7% and from 3.6% to 18.6%, respectively (Table A6).

We also separately incorporated the scores of each scale of the stigma scale into the model to obtain the ability of the scores of each to predict the PCS and MCS scores independently. Notably the NSE scale score improved the predictive ability of GH, VT, MH, and MCS scores to 21.2%, 21.2%, 17.3%, and 18.4%, respectively. This outcome means that for a categorical increase in the NSE scale (e.g., from general to agreed), a patient's MCS scores decreased by 1.042 [95% CI: 0.815, 1.270] points (Table 4).

Table 4: Associations between chronic hepatitis B related stigma scale and SF-36v2 scale scores (n=552)

Models	PCS Mean difference(95% CI)	R2	MCS Mean difference(95% CI)	R2
Multivariable model (MV)ᵃ		0.226		0.049
MV +Stigma		0.238		0.203
MV +Stigma-ED	-0.212(-0.377, -0.047)	0.236	-0.722(-0.955, -0.489)	0.116
MV +Stigma-NSE	-0.207(-0.376, -0.039)	0.235	-1.042(-1.270, -0.815)	0.184
MV +Stigma-PS	-0.113(-0.217, -0.009)	0.233	-0.452(-0.598, -0.305)	0.116
MV +Stigma-CO	-0.134(-0.319, 0.051)	0.229	-0.285(-0.554, -0.017)	0.057
MV +Stigma-SD	-0.161(-0.393, 0.070)	0.228	-0.752(-1.083, -0.421)	0.086

Abbreviations: PCS, physical component summary; MCS, mental component summary; ES, external discrimination: NSE, negative self-evaluation: PS, perceived stigma: CO, confidentiality; SD, secondary discrimination.

Table A5: Adjusted associations between SF-36 v2 scores with CHB-related characteristics and clinical indicators (n =552)

Predictors	PF Mean difference (95% CI)	RP Mean difference (95% CI)	BP Mean difference (95% CI)	GH Mean difference (95% CI)	VT Mean difference (95% CI)	SF Mean difference (95% CI)	RE Mean difference (95% CI)	MH Mean difference (95% CI)	PCS Mean difference (95% CI)	MCS Mean difference (95% CI)
Age, per 10 years	-1.604 (-2.973, -0.235) P=0.022	0.537(-1.642, 2.716) P=0.628	0.277(-1.566, 2.121) P=0.768	-1.364(-3.255, 0.526) P=0.157	-0.631(-2.434, 1.171) P=0.492	1.330(-0.399, 3.058) P=0.131	1.501(-0.652, 3.653) P=0.171	0.856(-0.836, 2.547) P=0.321	-0.696(-1.447, 0.055) P=0.069	0.988(-0.097, 2.073) P=0.074
Sex										
Male	Reference	Reference	Reference	Reference	Reference	Reference	Reference	Reference	Reference	Reference

Female	0.451(-2.323, 3.226) P=0.749	3.987(-0.434, 8.407) P=0.077	4.918(1.177, 8.660) P=0.010	-0.265(-4.062, 3.532) P=0.891	-4.622(-8.242, -1.002) P=0.012	2.678(-0.799, 6.156) P=0.131	1.216(-3.108, 5.540) P=0.581	-0.557(-3.955, 2.840) P=0.747	1.532(0.008, 3.056) P=0.049	-0.620(-2.804, 1.563) P=0.577
HBV disease stage										
CHB	Reference	Reference	Reference	Reference	Reference	Reference	Reference	Reference	Reference	Reference
CC	-7.643 (-11.392, -3.894) P<0.001	-6.245(-12.218, -0.271) P=0.040	-0.622(-5.669, 4.425) P=0.809	-5.340(-10.550, -0.130) P=0.045	-7.950(-12.917, -2.983) P=0.002	-3.136(-7.900, 1.628) P=0.196	-0.534(-6.466, 5.398) P=0.860	-3.241(-7.903, 1.420) P=0.172	-3.173(-5.228, -1.117) P=0.003	-1.143(-4.133, 1.848) P=0.453
DC	-5.182(-9.915, -0.448) P=0.032	-16.761(-24.309, -9.214) P<0.001	-7.931(-14.303, -1.559) P=0.015	-11.560(-17.700, -5.420) P<0.001	-11.794(-17.648, -5.941) P<0.001	-6.667(-12.281, -1.053) P=0.020	-13.251(-20.242, -6.259) P<0.001	-3.717(-9.210, 1.777) P=0.184	-5.077 (-7.672, -2.481) P<0.001	-3.778(-7.236, -0.187) P=0.039
HCC	-6.164(-13.130, 0.802) P=0.086	-8.559(-19.640, 2.523) P=0.130	-4.440(-13.817, 4.936) P=0.353	-8.476(-17.124, -0.171) P=0.055	-12.469(-20.713, -4.225) P=0.003	-13.086(-20.933, -5.179) P=0.001	-6.719(-16.566, 3.128) P=0.181	-1.872(-9.610, 5.865) P=0.635	-4.655(-8.474, -0.836) P=0.017	-1.907(-6.871, 3.056) P=0.451
AST		-0.031(-0.057, -0.004) P=0.025								
ALB	0.500(0.180, 0.819) P=0.002	0.626(0.114, 1.137) P=0.017	0.831(0.401, 1.261) P<0.001						0.335(0.160, 0.510) P<0.001	
ALP	-0.025(-0.053, 0.003) P=0.086	-0.051(-0.096, -0.006) P=0.026	-0.045(-0.083, -0.007) P=0.020	-0.048(-0.085, -0.011) P=0.011	-0.044(-0.079, -0.008) P=0.016	-0.098(-0.132, -0.064) P<0.001	-0.083(-0.125, -0.040) P<0.001	-0.060(-0.093, -0.027) P<0.001	-0.015(-0.030, 0.000) P=0.054	-0.043(-0.064,-0.021) P<0.001
Model R^2	R^2=0.166	R^2=0.159	R^2=0.145	R^2=0.086	R^2=0.098	R^2=0.133	R^2=0.076	R^2=0.036	R^2=0.054	R^2=0.049

Abbreviations: PF, physical functioning: RP, role physical: BP, bodily pain: GH, general health, VT, vitality: SF, social functioning: RE, role emotional: MH, mental health; PCS: Physical component summary; MCS: Mental component summary; CHB: chronic hepatitis B; CC: compensated cirrhosis; DC: decompensated cirrhosis: HCC: hepatocellular carcinoma; AST, aspartate aminotransferase; ALB, albumin; ALP: alkaline phosphatase.

Table A6: Associations between chronic hepatitis B related stigma scale and SF-36 v2 scale scores (n =552)

Models	PF Mean difference (95% CI)	R^2	RP Mean difference (95% CI)	R^2	BP Mean difference (95% CI)	R^2	GH Mean difference (95% CI)	R^2	VT Mean difference (95% CI)	R^2	SF Mean difference (95% CI)	R^2	RE Mean difference (95% CI)	R^2	MH Mean difference (95% CI)	R^2
Multivariable model(MV)a		0.166		0.159		0.145		0.086		0.098		0.133		0.076		0.036
MV +Stigma		0.192		0.184		0.165		0.216		0.219		0.194		0.147		0.186
MV +Stigma-ED	-0.421 (-0.722, -0.121)	0.179	-0.689 (-1.168, -0.211)	0.173	-0.666 (-1.069, -0.262)	0.163	-1.074 (-1.484, -0.664)	0.133	-1.068 (-1.458, -0.678)	0.148	-0.985 (-1.359, -0.610)	0.178	-1.002 (-1.473, -0.532)	0.108	-1.056 (-1.421, -0.691)	0.096
MV +Stigma-NSE	-0.557 (-0.862, -0.253)	0.19	-0.803 (-1.289, -0.317)	0.18	-0.585 (-0.997, -0.172)	0.16	-1.795 (-2.193, -1.397)	0.21	-1.635 (-2.017, -1.253)	0.21	-0.983 (-1.365, -0.601)	0.18	-1.211 (-1.687, -0.734)	0.12	-1.623 (-1.979, -1.267)	0.17
MV +Stigma-PS	-0.258 (-0.446, -0.069)	0.18	-0.386 (-0.688, -0.084)	0.17	-0.324 (-0.579, -0.069)	0.16	-0.791 (-1.046, -0.536)	0.15	-0.637 (-0.883, -0.391)	0.14	-0.501 (-0.738, -0.263)	0.16	-0.537 (-0.834, -0.239)	0.1	-0.734 (-0.961,-0.507)	0.11

MV +Stigma-CO	-0.202 (-0.540, 0.136)	0.17	-0.099 (-0.637, 0.439)	0.16	-0.383 (-0.838, 0.071)	0.15	-0.752 (-1.217, -0.288)	0.1	-0.77 (-1.212, -0.327)	0.12	-0.309 (-0.737, 0.120)	0.14	-0.065 (-0.599, 0.470)	0.08	-0.477 (-0.895, -0.060)	0.05
MV +Stigma-SD	-0.321 (-0.743, 0.102)	0.17	-0.677 (-1.348, -0.006)	0.17	-0.506 (-1.075, 0.062)	0.15	-1.324 (-1.900, -0.748)	0.12	-1.095 (-1.647, -0.543)	0.13	-0.848 (-1.380, -0.315)	0.15	-0.597 (-1.264, 0.071)	0.08	-1.372 (-1.884, -0.860)	0.09

Abbreviations: ED, External discrimination; NSE, Negative self-evaluation; PS, Perceived stigma; CO, Confidentiality; SD, Secondary discrimination; PF, physical functioning: RP, role physical: BP, bodily pain: GH, general health, VT, vitality: SF, social functioning: RE, role emotional: MH, mental health.

5. Discussion

The study shows that levels of mental HRQoL were more impaired than the physical HRQoL in the patients with CHB-related disease. Patients with CHB-related disease had lower vitality and worse general health and mental health, which indicated that the patients first presented symptoms of their own energy decline and all of the participants had serious emotional and psychological problems. With further progression of the disease (DC and HCC), the HRQoL was shown to worsen in all aspects. Previous studies also showed poorer HRQoL of DC or HCC patients [10-12]. Furthermore, a high stigma scale score was associated with worse HRQoL, which highlights the importance of paying attention to stigma in patients with CHB-related diseases in future studies.

HRQoL is the outcome reported by the patient and is related to patient's life expectancy. Patients with life-threatening or chronic diseases may adapt to the state of illness over a long period of time. An important regulator of this adaptation process is response transfer, including changes in intrinsic standard values and reconfiguration of HRQoL content [13]. Older patients tend to lower their life expectancy and have higher life satisfaction when their condition is stable. Our study shows that older patients have better mental HRQoL. According to the multivariate regression model that adjusted for age and sex, the physical HRQoL of the DC patients was worse than that of the HCC patients. Similar results have been seen in previous studies [14-15]. This outcome may be because patients in the decompensation stage have more symptoms. Three liver function characteristics related to HRQoL, AST, ALP and ALB levels, suggested that these levels may be considered important clinical indicators related to HRQoL in CHB-related disease patients.

Notably, the CHB-related disease patients have worse mental HRQoL status. This finding is not consistent with the results of a recent study in the United States, Canada and Italy [16-17], in which patients reported mental HRQoL similar to the general population but is similar to the early studies in China [18]. It can be inferred that Chinese patients with CHB-related diseases have more serious emotional and psychological problems. Our study shows that this is linked to the stigmatization of hepatitis B patients in China. Previous studies have shown that the vast majority of patients in China suffer from stigma due to hepatitis B and have strong negative emotional depression and stress [19-20].

Our study also focused on patients' stigma to evaluate the impact of stigma on patients' HRQoL. In the multivariate regression model, sociodemographic and clinical factors had little impact on patients' psychology, and the explanatory variation of mental HRQoL increased from 4.9% to 20.3% after the stigma scores were added to the independent variables. The explanatory variation of mental health and vitality increased from 3.6% to 18.6% and from 9.8% to 21.9%, respectively. Patients' negative self-evaluation, external discrimination and perceived stigma were negatively correlated with mental HRQoL. This showed that patients with CHB-related diseases have lower self-value, negative self-knowledge and inner humiliation, and patients' perceived social public prejudice and rejection of the patient. In addition, a previous study has also showed that psychological intervention for patients with CHB-related diseases has a positive effect and improves HRQoL [21]. A study in the United States showed that among patients with chronic hepatitis B, those who received social support had better mental HRQoL, and those who needed medicaid were more likely to have poor HRQoL [22]. This suggests that psychological intervention and social support for patients with CHB-related diseases will not only protect them from stigma but also improve their HRQoL. We also found that stigma increased the degree of variation in general health, which is correlated with physical HRQoL, from 10.0% to 22.5%. This finding indicated that the stigma of CHB-related disease patients would also have impact on their own physical HRQoL.

6. Limitations

Our study has some limitations. The subjects were recruited from tertiary hospitals. These patients may have a more serious condition than those in tertiary hospitals. However, the hierarchical medical system is not strictly implemented in China, and most patients with mild symptoms tend to go to tertiary hospitals for treatment. Furthermore, lack of adjustment for sociodemographic characteristics may have biased the results, although the results were partly corrected by age and sex adjustment.

7. Conclusion

Early-stage CHB-related diseases affected mental HRQoL, while advanced stages (DC and HCC) affected overall HRQoL. All aspects of stigma have a certain impact on the HRQoL of patients with CHB-related diseases; there is effect on mental HRQoL, but a weak effect on physical HRQoL. The negative self-evaluation of patients

has a greater influence on HRQoL. This outcome suggests that we should pay attention to the problem of CHB-related disease patient stigma, especially the psychological problems of patients with lower self-worth due to stigmatization.

8. Funding

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