Review Article

# A Review of Psychosocial Issues in Patients with Chronic Hepatitis B

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**Abstract**

Psychosocial issues and health-related quality of life (HRQOL) are important components of care in patients diagnosed with chronic hepatitis B (CHBV).

In this review, we searched Medline, ISI Web of Knowledge, Google Scholar and the American Association for the Study of Liver Diseases (AASLD) website (until January 2012) using relevant terms and we categorized the retrieved content into three areas: HRQOL, mental health, and psychosocial issues such as stigma and coping.

Increasing severity of CHBV leads to a decline in HRQOL. Cirrhosis worsens HRQOL, whereas treatment and psycho-education improves it. Frequency of mood disorders seems to be increased in patients with CHBV, although not all studies have shown this trend. Some factors such as alcohol consumption and low social support negatively impact patients' mental health. Those with CHBV generally have better HRQOL and mental health than their hepatitis C (HCV) counterparts. Patients with psychiatric disorders, particularly those with prolonged institutionalization, have a generally higher risk of acquiring CHBV infection compared to the general population. Robust studies regarding the stigma in patients with CHBV are lacking, although some studies have suggested a higher degree of perceived stigma in these patients.

HRQOL and mental health are significantly affected in CHBV patients, particularly in those with more severe forms of the disease. There are few studies that addressed the effects of intervention in CHBV patients with psychosocial problems. Other subjects necessitating additional research include stigma, coping mechanisms, and other less common, yet important psychosomatic disorders.

**Keywords:** Anxiety, chronic hepatitis B, depression, health-related quality of life, stigma

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## Introduction

Chronic diseases are associated with a significant burden of psychosocial problems including impaired health-related quality of life (HRQOL), depression, anxiety, and other psychological impairments.[1–4] In cases where these chronic conditions stigmatize the patient, psychological impairment becomes more pronounced. This is particularly seen in infectious diseases associated with high risk behaviors, highly contagious diseases, and psychiatric disorders.[5–9] Chronic hepatitis B (CHBV), as one of the most common causes of liver disease,[10] is associated with a high psychosocial burden.[11,12] Moreover, complications of advanced liver disease may be associated with poorer HRQOL irrespective of the cause of the liver involvement.

Few studies have addressed the psychosocial burden of CHBV when compared to other chronic infectious diseases such as human immunodeficiency virus (HIV) and hepatitis C (HCV).[13] Data for psychological problems such as anxiety and depression are particularly scarce, and most focus on the HRQOL of these patients.

In the present review we attempted to integrate the literature on the psychosocial concerns among CHBV patients with the intent to provide a clearer picture of their psychological and HRQOL issues.

We performed a literature search with terms (Hepatitis B) and [(psychosocial) or (emotional) or (anxiety) or (depression) or (stigma) or (psychological) or (psychiatric) or (psychiatry) or (psychology) or (social) or (quality of life)] in Medline, ISI Web of Knowledge, Google Scholar and the American Association for the Study of Liver Diseases (AASLD) website (until January 2012). Some articles in Google Scholar were in Chinese and irretrievable. Due to the uncertainty regarding rigorous peer review, we included only articles that provided a clear explanation of their methods in the abstract and those which were unlikely to be biased (descriptive studies). Other than the above mentioned Chinese articles, we did not consider language to be a limitation in our search process.

## Health-related quality of life (HRQOL) in chronic hepatitis B (CHBV) patients

### Overview

Apart from being a marker of patients' mental and physical function, HRQOL measurements serve as an important outcome in clinical trials and for cost effective analyses of treatment modalities.[14–16] HRQOL should be measured by using appropriate instruments that have sufficient reliability, validity and suitable factor structure. Measurements of HRQOL should be capable of catching the differences between stages of a specific disease. Instruments that measure HRQOL can be placed into two general subcategories: generic and disease-specific. Generic instruments allow for a comparison between patients diagnosed with the tar-

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get condition and those without. Generic instruments fail to catch disease-specific outcomes, whereas disease-specific instruments are sensitive to specific clinical conditions. Table 1 summarizes the most important HRQOL tools used in chronic hepatitis.[17–23]

### Effect of severity of CHBV on HRQOL

As shown in Table 2, several studies have addressed the differences in HRQOL that exist between varying severities of CHBV, which can range from an asymptomatic carrier to decompensated cirrhosis and hepatocellular carcinoma (HCC). Differences between inactive carriers and normal subjects are perhaps the most debatable. By using EQ-5D and SF-36, Ong et al.[11] have evaluated HRQOL of patients in different stages of CHBV, from chronic inactive hepatitis (CIH) to HCC. For comparison, these researchers also included two groups, hypertensive patients and healthy control subjects from the same area. Their study showed that HRQOL decreased as the disease progressed to its more severe forms. However, patients with CIH had similar scores to healthy controls. After controlling for the effects of age, sex, ethnicity, and educational level, the authors found that scores from the subscales of bodily pain and general health were significantly lower in asymptomatic carriers than healthy controls. In another study, Lam et al.[12] compared 520 CHBV patients (including 156 CIH patients) with population normative data. They found no difference in the mental component summary score of SF-36 (MCS) between CIH patients and controls, whereas there was a significant difference in physical component summary (PCS) scores between these two groups.

Although the use of population norms for comparison may seem reasonable, there are regional and cultural differences within a country that can only be taken into account by inclusion of the normal population from the same region. Using population normative data, several studies have found lower scores in a few domains of HRQOL in patients with CIH when compared with control subjects.[24–27] Discrepancies between the abovementioned studies can be explained as differences between patients with regards to their baseline characteristics which might have affected HRQOL. Moreover, except for the study by Ong et al.[11] that controlled for these variables, other researchers have paid less attention to controlling for possible confounding factors. Additionally, HRQOL instruments vary with regards to their factor structure and sensitivity to differences.

Different disease stages can affect HRQOL in different degrees. In a well-designed study, Ong and colleagues have shown that CHBV patients with chronic active hepatitis (CAH) had scores close to patients with compensated cirrhosis.[11] All had better HRQOL when compared with decompensated cirrhosis and HCC. Post-transplant patients showed a trend toward improvement in their HRQOL when compared with patients with decompensated cirrhosis and HCC. PCS was generally more impaired than MCS in patients with HCC and decompensated cirrhosis. Using SF-36 and Chronic Liver Disease Questionnaire (CLDQ), Lam et al. did not find any significant difference in most subscales (other than worry) between patients with CIH and those with CAH.[12] As confirmed by several other studies, in most subscales CIH patients showed significantly better HRQOL than those with HCC and cirrhosis. This difference was also observed between the CHBV group and patients with cirrhosis and HCC in some of the subscales, most of which focused on PCS. In a multinational study of patients from six countries, Levy and colleagues

**Table 1.** Features of disease specific quality of life questionnaires used for patients with hepatitis.

| Questionnaire / Developer/ year/ref. number | Number of questions/ Time needed to complete | Subscales | Reliability | Validity |
|---|---|---|---|---|
| Hepatitis Quality of Life questionnaire/ Bayliss et al./1998/[18] | 69 (past four weeks)/ NA | All eight SF-36 subscales, sleep, health distress, CHC distress, CHC limitations | $\alpha$ = 0.81–0.94 | Related subscale: > 0.6<br>Unrelated subscale = 0.33 |
| Chronic Liver Disease Questionnaire/ Younossi et al./ 1999/[17] | 29 seven-point Likert scale items (past two weeks)/ 10 min | Fatigue, emotional function, worry, abdominal symptoms, activity, systemic symptoms, sleep (new subscale) | $\alpha$ = 0.72–0.95<br>Test-retest = 0.58–0.79 | Related subscales = 0.69–0.85<br>Unrelated subscales: 0.33–0.48 |
| Liver Disease Quality of Life Questionnaires/ Gralnek et al./ 2000/[21] | 111 (past four weeks)/ 38.3 min | All eight SF-36 subscale, Symptoms of liver disease, Effects of liver disease , Concentration, Memory, Quality of social interaction<br>Health distress, Sleep , Loneliness , Hopelessness, Stigma of Liver disease , Sexual functioning, Sexual problems | $\alpha$ = 0.62–0.95 | Worse HRQOL is associated with worse severity |
| Liver disease symptoms index/ Unal et al./ 2001[19] | 12 (past one week)/ <6 min | Itching, joint pain/discomfort, pain in the upper abdomen, drowsiness, sleeping during the day, lack of appetite, fear of complications | $\alpha$ = 0.79–0.86<br>Test-retest = 0.72–0.84 | Unrelated subscales: < 0.6 |
| Liver disease symptoms index 2.0/ Van der Plas et al./ 2004/[22] | 18 (past one week)/ NA | Itch, Joint pain, Pain in the right upper abdomen , Sleepiness during the day, Worry about family situation, Decreased appetite<br>Depression, Fear of complications, Jaundice | $\alpha \geq 0.79$<br>Test-retest = 0.55–0.99 | Related subscales = 0.52–0.8 |
| Hepatitis B Quality of Life Questionnaire 1.0/ Spiegel et al./ 2007/[20] | 31/6 min | Psychological wellbeing, Anticipation anxiety, Vitality, Stigma, Transmissibility, Vulnerability, Viral response | $\alpha$ = 0.73–0.96<br>test-retest = 0.96 | Related subscales = 0.55<br>Unrelated subscale < 0.4 |

SF-36 = short form health survey-36; CHC = chronic hepatitis C; NA = not available

**Table 2.** Summary of most important studies of health related quality of life in patients with hepatitis B.

| Study/year/country/ref. number | Groups (instruments used) | Main results | Comments |
|---|---|---|---|
| Foster et al./ 1998/ England /[33] | 72CHC/ 32CHBV/17 healthy controls(SF-36) | CHC patients showed significant reduction in both mental and physical aspects, while CHBV only showed reduction in mental aspects of HRQOL | No effect of mode of acquisition, inflammation grade, and severity of hepatitis was found on HRQOL in CHC patients |
| Kanwal et al./ 2005/ USA /[94] | 122 HIV-CHBV/ 279 HIV-CHC/ 1493 HIV (HC-SUS) | Scores of HRQOL were similar in all groups. | |
| Bao et al./ 2007/ China /[37] | 20 CHBV/ 106 cirrhosis (including CHBV)/ 160 healthy controls(CLDQ, SF-36) | Both CHBV patients and cirrhotic patients had lower scores on SF-36 and CLDQ compared with healthy controls | MHE significantly reduced the score of SF-36 but not CLDQ |
| Bondini et al./ 2007/ USA /[32] | 68 CHBV/ 60 CHC/ 18 PBC/ normative data(CLDQ, SF-36, HUI) | Control subjects and CHBV patients had better HRQOL than CHC and PBC patients, but did not differ from each other. Only HUI scores was lower in CHBV patients compared to controls. | Patients with cirrhosis had significantly lower scores on physical health and HUI, but not CLDQ and mental health scores than patients without cirrhosis. |
| Dan t al./ 2007/ USA /[30] | 56 CHBV/ 75 CHC/ 106 NAFLD(CLDQ) | CHBV patients had significantly better HRQOL scores than the other two groups. NAFLD had the poorest HRQOL. CHC and CHBV differ only in their abdominal and activity subscales | |
| Heidarzadeh et al./ 2007/ Iran /[95] | 15 CHBV/59 CHC(CLDQ) | No difference between CHC and CHBV in HRQOL | The results are limited by the small sample size |
| Dan et al./ 2008/ USA /[96] | 51 CHBV/ 41 CHC/ 33 cholestatic liver disease/ 15 other liver diseases(SF-6D, HUI-2) | CHBV patients had the best scores, followed by CHC and cholestatic liver disease, and other liver diseases | Cirrhosis, higher Child-Turcotte-Pugh scores had negative impact on HRQOL |
| Levy et al./ 2008/ US, UK, Canada, Spain, Hong Kong, China /[28] | 600 CHBV in different stages/ 534 healthy controls(LDQOL) | Infected respondents had significantly lower scores on health utilities than non-infected respondents | |
| Marcellin et al./ 2008/ Multinational /[97] | 448 CHBV/ 791 CHC (both treated with PEG-INFα2 (SF-36) | More drop was seen in PCS scores of CHC compared with CHBV. No difference was observed in MCS scores. | Data were adjusted for age and gender |
| Nokhodian et al./ 2008/ Iran [98] | 61 CHBV/ 60 CHC (CLDQ) | Most of the items showed lower score in CHC patients compared with CHBV | |
| Ong et al./ 2008/ Singapore /[11] | 156 asymptomatic carrier/ 142 CHBV/ 66 compensated cirrhosis/ 24 decompensated cirrhosis/ 22 HCC/ 22 post-transplant/ 93 hypertensive controls/ 108 normal controls(SF-36, EQ-5D) | Asymptomatic carriers and normal controls had similar HRQOL scores which were better than other patients (including hypertensive controls) | HRQOL progressively declines as the CHBV progresses. This progression was evident first in the mental and then in the physical dimension. |
| Svirtlih et al./ 2008/ Serbia /[31] | 167 CHC/ 60 CHBV/ 75 control All patients are treatment naïve(SF-12) | Lower HRQOL in patients than in controls and in cirrhotic patients compared with non-cirrhotic patients. No difference between CHC and CHBV in both mental and physical aspects | Age has negative impacts on HRQOL |
| Tan et al./2008/ Singapore /[25] | 108 chronic carriers/ population norms(HQOQ) | Only lower scores on SF compared to normal population | Age, gender, family history, and employment have different effects on different domains |
| Wah-Yun et al./ 2008/ Malaysia /[99] | 409 CHBV/ 74 Cirrhosis with or without HCC(SF-36) | No difference between two groups in all domains | |
| Woo et al./ 2008/ Canada /[38] | 195 CHBV/ 73 compensated cirrhosis(EQ5D, SF-36, HUI-3) | No difference between CHBV group and population norms. Lower HRQOL scores in CC compared with CHBV | |
| Altindag et al./ 2009/ Turkey /[24] | 30 carrier/ 30 CHBV/ 30 healthy controls(SF-36) | Lower scores in all domains in CHBV compared with healthy controls. Lower scores on BP, VT, PF in carriers compared to controls. Lower scores on RE in CHBV compared to carriers | |

| | | | |
|---|---|---|---|
| Lam et al./ 2009/ Southern China /[12] | 156 uncomplicated CHBV/ 102 impaired liver function/ 139 cirrhosis/ 123 HCC/ Hong Kong population norms (SF-36v2, CLDQ, SF-6D) | Significantly lower HRQOL in CHBV patients than controls, cirrhotic patients had the lowest HRQOL and were very close to patients with HCC. | Advanced stage of CHBV illness, anti-viral treatment, bilirubin level, psychological co-morbidity, younger age and female were associated with poorer HRQOL. |
| Karaivazoglou et al./ 2010/ Greece /[34] | 45 CHBV/ 39 CHC/ normative database(SF-36) | CHBV patients had similar HRQOL to CHC, and both groups had poorer HRQOL than general population | Age and fibrosis stage correlated with PCS, ALT, Fatigue and depression correlated with MCS |
| Tasbakan et al./ 2010/ Turkey /[27] | 128 carrier/ 28 CHBV/ population norms(SF-36) | No difference between carrier and CHBV after controlling for education other than in PF. Score in all domains other than VT and PF was lower in HBsAg+ compared with healthy controls | Education and PF explained most of the difference between carriers and CHBV patients |
| Modabbernia et al. /2011/ Iran /[35] | 31 CHBV/ 40 CHC(SF-36) | CHBV patients had significantly better physical health compared with CHC patients. The mental health was not different between two groups. | The patients were untreated without history of drug abuse, psychotic disorders, alcohol abuse and were non-cirrhotic |

CHC = chronic hepatitis C; CHBV = chronic hepatitis B; SF-36 = Short Form health survery-36; HRQOL = health related quality of life; HC-SUS = HIV Cost and Services Utilization Study; CLDQ = Chronic Liver Disease Questionnaire; HUI = Health Utility Index; PBC = Primary biliary cirrhosis; NAFLD = Nonalcoholic fatty liver disease; LDQOL = Liver Disease Quality of Life Questionnaire; PCS = Physical Component Summary of SF-36; PEG-INF α2 = Pegylated-interferon α2; EQ-5D = standardized instrument of health status developed by the EuroQol; HCC = hepatocellular carcinoma; SF-12 = Short Form health survey-12; HQOQ = Hepatitis Quality of Life Questionnaire; BP = Bodily Pain subscale of SF-36; , VT = Vitality subscale of SF-36; , PF = Physical Functioning subscale of SF-36; RE = Role Emotional Subscale of SF-36; MCS = Mental Component Summary of SF-36; ALT = Alanine aminotransferase; HBsAg = Hepatitis B surface antigen.

used standard gamble utilities to evaluate 534 CHBV patients and related conditions (cirrhosis, HCC, transplantation) to 600 uninfected subjects.[28] The health statuses with the highest mean were compensated cirrhosis, CHBV without cirrhosis, and post-transplant patients one year after transplantation.

To conclude, although in some domains patients with CIH have lower HRQOL than the general population, their HRQOL is less impaired than patients with active CHBV, and approximates the normal population. Accordingly, treating patients with active disease to turn active viral disease into CIH may improve their HRQOL significantly. There is a poorer HRQOL in patients with decompensated cirrhosis and HCC compared to the milder forms of CHBV; this difference is more pronounced in areas related to physical health. Asymptomatic carriers have better HRQOL compared with compensated cirrhosis and CHBV patients in some of the subdomains. HRQOL of post-transplant patients show gradual improvement over time, although additional studies are needed to address this issue in greater detail.[29]

### HRQOL in CHBV patients compared to other diseases

Several studies compared HRQOL between CHBV patients and those with other liver diseases. Most data focused on a comparison between CHBV and HCV patients. In one study researchers used CLDQ to compare CHBV (n = 56), HCV (n = 75), and non-alcoholic fatty liver disease (NAFLD, n = 106) patients.[30] Scores from all subscales (other than worry) were higher in CHBV patients compared to those with NAFLD. There was no difference in most subscale scores between CHBV and HCV patients, however scores from the activity and abdominal subscales were significantly lower in HCV than in CHBV patients.

In another study the authors compared HRQOL of 167 chronic HCV and 60 CHBV patients to 75 healthy control subjects using the Short Form Health Survey-12 (SF-12).[31] The results of this study showed significantly lower SF-12 scores in HCV and CHBV patients compared with healthy controls; no difference was found between the CHBV and HCV groups. Of note, HCV and CHBV patients differed in terms of age, marital status and possibly cirrhosis (not reported in the study) which might have potentially affected the results. Cirrhosis is associated with more physical impairment, however while the majority of the study patients did not have cirrhosis, the authors have observed more physical than mental impairments. A possible explanation might be the exclusion of patients with mental problems and the higher proportion of HCV patients, which per se may be associated with higher physical disabilities. However, in contrast, another study that compared the HRQOL of CHBV, HCV, and primary biliary cirrhosis (PBC) patients to normal controls observed better HRQOL in CHBV patients compared to HCV and PBC patients.[32]

Most studies that compare HRQOL between HCV and CHBV have limitations due to failure to control for comorbidities that accompany HCV. To address this issue, Foster et al.[33] compared 72 chronic HCV patients to 30 CHBV patients and 17 healthy controls using SF-36. Patients with multiple viral infection, patients taking antiviral medications, and those with cirrhosis were excluded. CHBV patients showed significant reduction only in their mental subscale scores compared to control subjects. In contrast, chronic HCV patients showed significant impairment in both physical and mental domains. Controlling for history of drug abuse, ALT levels and degree of inflammation did not affect the results. Karaivazoglou et al.[34] have conducted a similar study on 45 CHBV and 39 chronic HCV patients using SF-36. Excluded were patients with recent history of drug or alcohol abuse, cirrhosis, concomitant HIV infection, interferon treatment and physical comorbidities. Baseline characteristics of the patients, stage and grade of liver disease, and liver enzymes were similar between the two groups. There was no difference in any of the SF-36 subscales between the HCV and CHBV groups. A third study by our group elucidated the role of brain-derived neurotrophic factor in impairment of HRQOL amongst HCV patients. In this study, we attempted to control for most factors that might influence HRQOL

in patients with viral hepatitis.[35] A homogenous group of 40 male HCV patients and 31 male CHBV patients were studied. Alcohol or drug abuse within six months of the study, cirrhosis, co-infection with HIV and current antiviral medications were exclusion criteria. We administered SF-36 and the Hospital Anxiety and Depression Scale to all patients. Depression, anxiety and MCS did not differ significantly between the groups, whereas in SF-36 the PCS was significantly lower in patients with HCV compared to those with CHBV. Fibrosis score did not correlate with the scores of the mentioned scales.

In summary, most studies agree that HRQOL in CHBV patients is better than HRQOL in patients with other liver diseases. In addition, most research has shown poorer HRQOL (particularly in the physical health-related subscales) in HCV patients compared to CHBV. This is further supported by a magnetic resonance spectroscopic study which has shown no difference in the brain choline/creatine ratio between CHBV patients and healthy controls. However, HCV patients did show an abnormal pattern of cerebral metabolites compared with both the healthy control group and CHBV patients, even after taking into consideration the higher rate of IV drug abuse among HCV patients.[36]

### Factors affecting HRQOL in CHBV

One of the most important determinants of HRQOL in CHBV patients is disease severity. Generally, HRQOL worsens with increasing disease severity.[11,12,37–39] As mentioned, patients with cirrhosis have poorer HRQOL than non-cirrhotic patients. Amongst patients with cirrhosis, those with minimal hepatic encephalopathy (MHE) have poorer HRQOL than patients without MHE.[37] A consistent pattern amongst all studies is the improvement of HRQOL in CHBV patients following treatment.[40–42] In a prospective study, 2856 Korean subjects with CHBV were administered the CLDQ and EQ-5D (EuroQol) at baseline and 24 weeks after antiviral treatment. Scores in all domains of HRQOL improved significantly after treatment. This improvement was more pronounced in females, HBeAg positive subjects and those without comorbidities, whereas it was less evident in patients with advanced liver disease. Improvement in HRQOL was strongly associated with viral response.[43] Other determinants of HRQOL in CHBV are less well understood. One important pitfall in most studies is the failure to consider and control for confounding variables.

Interventional studies pertaining to psycho-education in CHBV patients are scarce. A randomized trial of four sessions of psycho-education in patients with viral hepatitis has shown modest effect of psycho-education on HRQOL scores.[44] In a semi-experimental study, the effect of an educational program on chronic viral hepatitis patients who were under treatment by interferon was investigated. After a brief educational program, patients were followed for 28 weeks. HRQOL significantly improved in the experimental compared to the control group. Importantly, the rate of treatment withdrawal was four times more in controls compared to the experimental group.[45]

## Psychiatric disorders and symptoms among CHBV patients

### Psychiatric disorders in CHBV patients

Studies of psychological disturbances in CHBV patients are mostly limited to anxiety and depression. Most studies have used self-report questionnaires to assess anxiety and depression, however, few studies have utilized structured clinical interviews. Atesci et al.[46] used the Beck Depression Inventory (BDI), State-Trait Anxiety Inventory (STAI), DSM IV Axis I (psychiatric disorders) and Axis V (global functioning assessment) to compare 43 CIH patients with 43 healthy matched control subjects. These researchers showed that psychiatric disorders (particularly major depression), anxiety and depressive states, and poor global functioning were more common in CIH patients than in healthy controls. There was a higher rate of psychiatric disorders in those who had been diagnosed with CHBV within three months of the interview. The higher degree of perceived stigma and concern about the consequences of CHBV might partially explain the higher rate of mood problems among recently diagnosed patients.[47] In another study, HCV patients were compared with CHBV patients and healthy controls using structured clinical interviews.[48] The rates of all psychiatric disorders were higher in patients with viral hepatitis than in normal controls, while HCV and CHBV groups showed similar rates. Other studies have used self-report measures to assess the anxiety and depression in CHBV patients. In a large study, Weinstein et al.[49] compared retrospective data of 504 HCV patients, 190 CHBV patients, and 184 patients with NAFLD. Diagnosis of depression was based on patient self-report and confirmed by history of antidepressant use. The researchers noted the presence of depression in 4% of CHBV patients compared to 27% of NAFLD patients and 30% of HCV patients. However, their study was limited by a heterogeneous distribution of baseline characteristics and comorbidities in each of the three groups. Furthermore, because of method of determining depression, the authors possibly overlooked more subtle, but still clinically significant depression.

As mentioned above, two studies by Foster et al.[33] and our group[50] both showed slight differences in the scores of mental health measures between HCV and CHBV patients. In a third study on a matched population of CHBV and HCV patients, the authors found a trend toward significant difference in depression scores of BDI between HCV and CHBV patients.[34] Another study evaluated 30 patients with CAH, 30 patients with CIH, and 30 control subjects using BDI.[24] Severe depression (score $\geq$ 17) was observed as follows: CAH (20%), CIH (13.3%), and healthy controls (3.3%). Other studies of mental health in CHBV were limited by small sample size, absence of a comparison group, and inaccurate measurement or analysis methods.[47,51–54]

The association between CHBV and other psychiatric and psychosomatic disorders are less well studied. Adak and coworkers studied 50 CIH HBsAg+ patients and 50 control subjects matched for age and sex. Fibromyalgia and fibromyalgia-associated symptoms as well as variety of psychosomatic problems were more common among the patients compared with controls.[55]

One of the most deficient areas in the study of psychosocial issues of CHBV patients is study of children. Li et al. have compared more than 300 CHBV high school students with more than 600 healthy students using Symptom checklist-90 (SCL-90).[56] They found higher levels of depression, anxiety and labile emotional states in patients compared with controls. The psychological distress in these children not only affects the patient, but also negatively impacts their parents.[57] However, in another small study, there was no difference in scores of anxiety and depression according to the STAI and children depression inventory between patients with CIH, CAH, and healthy controls.[58] Generally, CHBV patients have poorer mental health when compared

with healthy subjects. With increasing disease severity there is a decline in mood state. However, CHBV patients may have better mental health than HCV patients, which may be due to the higher rate of comorbidities in HCV patients such as higher rates of interferon treatment, alcohol and illicit drug abuse, and possibly a more vulnerable personality. Controlling for these factors can eliminate most differences between HCV and CHBV patients.[33,34,50,59]

### Determinants of psychiatric symptoms in CHBV patients

Several factors are associated with anxiety and depression in CHBV patients. Weinstein et al.[49] have found alcohol consumption to be the sole predictor of clinically significant depression in these patients. Kunkel and coworkers have shown an association between BDI scores, higher psychosocial stress, poorer general functioning, and higher aminotransferase levels. However they stated that patients were aware of their aminotransferase levels, which might have influenced their BDI scores.[52] Social support seems to be associated with better mental health and HRQOL in these patients.[23] Although a few studies have addressed predictors of anxiety and depression in CHBV patients, there is obviously a lack of methodologically robust data. A multiple regression analysis that considers several clinical, socioeconomic and baseline variables together can certainly solve a part of this important puzzle.

### Rate of CHBV infection among psychiatric patients

Substance abuse and high-risk behaviors are frequent companions of psychiatric disorders. Patients with severe psychiatric disorders are at increased risk for poverty which in turn, raises the risk of acquiring infections and possibly translates into a higher rate of CHBV infection among psychiatric patients. There is great variability among the findings of different studies with regards to the rate of CHBV infection among the patients with psychiatric disorders.[60–81] The prevalence rate is highly variable among different studies that have been conducted in the same county. For example, according to different reports from Spain the prevalence rate of CHBV infection in institutionalized mentally handicapped subjects is 1.8% to more than 80%.[72] This might reflect the differences in baseline characteristics (most importantly age) as well as type of institution (closed or open), and changes in the prevalence rate of CHBV in the general population over time.[72] Xue-Run et al.[82] evaluated rate of CHBV infection in 3896 hospitalized patients with psychosis and 4191 normal controls. The infection rate of CHBV in patients was 60.99%, whereas in healthy controls it was 44.35%. Chang and colleagues studied 780 Taiwanese patients and found a prevalence of 18.1% of HBsAg+ which was similar to the Taiwanese general population.[83] Table 3 provides a brief summary of the most recent studies in this area. Most studies have shown an increased prevalence of CHBV infection in patients with mental disorders or disabilities compared to the general population. One risk factor that is consistent among studies is the prolonged duration of hospitalization or institutionalization.[61,72,75,76,79] The risk of acquiring CHBV in psychiatric institutions is declining because of immunization, but this issue still requires attention, particularly in developing countries.

## Other psychosocial issues

Stigma can significantly affect patients' lives, causing decreased HRQOL.[9,20,84] Studies of stigma in CHBV patients are one of the most deficient areas in the scientific literature. An Australian study has suggested that perceived stigma for CHBV might be lower than that of HIV or HCV.[85] Li et al. [86] studied 343 Chinese Canadian patients with CHBV stigma scales, and showed that the overall mean scores favored a higher stigma perception. In a multiple regression analysis they observed that older age and lack of acquaintances with CHBV were significant predictors of stigma scores. Stigma might significantly affect social life and HRQOL[87]; hence, its interference with treatment compliance and seeking treatment for serious conditions can be possibly detrimental. In a recent survey in the United States more than 80% of CHBV patients stated that they had chosen a support group because non-infected people "don't understand" them.[88] Thus, improving knowledge in the non-infected population might possibly improve patients' overall mental health and lessen their perceived stigma.[87] Stigma might significantly affect disclosure of the infection.[85,89] The degree of perceived stigma varies among different socioeconomic and cultural backgrounds[90] and can even affect the patients' participation in studies as has been shown by the lower enrollment of Asian subjects compared to Caucasians in one study.[91] Disclosure of the diagnosis of CHBV might be also stressful for patients' families, as shown by a study on mothers of children with CHBV.[57,92] In a small study, 19 CHBV patients were interviewed regarding their most important concerns. While more than 50% of them expressed concern about infecting others, only 36.1% were concerned of being stigmatized. A major drawback to this study was the lack of a valid measurement instrument. In addition, while the term social stigma might be used for determining stigma, other factors such as loss of job or fear of infecting others (which had been asked in this study as separate entities) could also be categorized as stigma.[93]

Coping is the mental attempt of an individual to resolve a perceived incongruity between external or internal demands, and personal capabilities. One study has suggested that parents of CHBV patients used both personal and social resources more often than parents of normal individuals. Although this study showed little difference in social support scores between parents of the two groups, parents of CHBV patients tended to have less close friends and less support by their friends.[92] This could be particularly worrisome, because lower social support can predispose mothers to higher stress burdens and increased risk of developing psychiatric disorders. There are few rigorous studies on the coping mechanisms in CHBV patients.

## Conclusions

HRQOL is significantly affected in CHBV patients, particularly in those with more severe forms of the disease. Prevention of disease progression with early treatment or liver transplantation can certainly improve HRQOL. Even though some antiviral medications decrease HRQOL during the acute treatment period, the HRQOL of CHBV patients improves after completion of antiviral treatment. Most interventional studies in this area have addressed HRQOL as a secondary outcome and this may affect their robustness. Studies which provide strong evidence on effect of psychoeducational intervention on patient HRQOL are lacking.

Psychiatric disorders and psychological impairment (particularly anxiety and depression) are common among CHBV patients, and identifying accompanying conditions such as high psychological stress and alcoholism may decrease the rate of patients' psychiatric problems. However, more rigorous studies are neces-

**Table 3.** Overview of most recent studies of prevalence rate of HBV infection in patients with mental problems (For a comprehensive review of older studies of prevalence rates in mentally retarded subjects see Vellinga et al.[100]).

| Author/year/ country/ref. number | Mental illness / Sample size/ study year | Prevalence rate of HBcAb and / HBsAg in the patients | Prevalence rate of markers in the general population | Comments |
|---|---|---|---|---|
| Cramp et al./ 1996/ England/[75] | Mental retardation /101/ (1987–1994) | 42.6%/ 14% | NA | Inpatient, and male subjects were at higher risk |
| Marena et al. / 1996/ Italy/[79] | Mental handicap /510/ 1993 | 57.1%/ 5.1% | 5% | Sex, age at admission, length of stay, and unsafe behavior were associated with higher risk |
| Eveillard et al./ 1999/ France/[80] | Psychiatric /327/ 1995–1997 | NA/2% | NA | |
| Asensio et al./ 2000/ Spain/[72] | Mental retardation /171 (1994) | 81.3%/ 8.8% | One fifth of the prevalence rate in the patients | Longer stay in the institution is associated with higher rates of seropositivity |
| Rosenberg et al./ 2001/ USA/[77] | BD, MDD, schizophrenia ± substance abuse /931 (1997–1998) | 23.4% (without major risk factors, 8.5%) | 3.9% | Inpatient status has no effect on the prevalence |
| De Souza et al./ 2004/ Brazil/[78] | Psychiatric illness/ down syndrome /433/1999–2001 | 24.3% psychiatric disorder without substance,16.9% psychiatric disorder with substance, 12% in down syndrome/ 2.1% in psychiatric disorder without substance abuse, none in other groups | NA | Multiple hospital admission was associated with higher prevalence rate |
| Esquivel et al. /2005/ Mexico/[73] | Schizophrenia, delusional disorder/ Down Syndrome /99/ 1995–1996 | HBcAb NA/ 12.1% are either HBsAg positive (7%) or HBsAb positive (5.1%) | 0.08% in healthy blood donors | Older age was associated with higher risk of infection |
| Chlabicz et al./ 2006/ Poland/[76] | Mental retardation and psychiatric disorders /691/ NA | HBcAb NA/ HBsAg 9.6% in mental retardation/ 2% in psychiatric subjects | 1–2% | The prevalence was higher in young male subjects with longer stay in the institution, and younger age at the diagnosis |
| Xue-Run et al./ 2006/ China/[82] | Psychosis /3896/ 2003-2005 | 60.99%/ 13.65% | 44.35% | |
| Kakisi et al./ 2009/ Greece/[61] | Psychiatric inpatients /803/ 2005–2007 | NA/ 2% | 3% in general population/ 2.7% in non- psychiatric settings | Longer hospitalization was associated with higher risk of HBsAg + (4%) |
| Mamani et al./ 2009/ Iran (Hamedan)/ [81] | Schizophrenia, behavioral disorders and others /170/ 2006 –2007 | NA/ 1.2% | | |

HBcAb = hepatitis B core antibody; HBsAg = hepatitis B surface antigen; NA = not available; BD = bipolar disorder; MDD = major depressive disorder; HBcAb = hepatitis B core antibody.

sary in order to find determinants of psychiatric symptoms in patients with CHBV. One important research area in these patients is personality traits and disorders which may predispose patients to high risk behaviors and subsequent infection with CHBV. Psychological and behavioral intervention can be potentially helpful in improving both psychological health and treatment adherence of CHBV patients.

Patients in psychiatric institutions are at increased risk for infection with viral hepatitis. Immunization, continuous surveillance, education of those who have psychiatric disorders and their families, and decreasing the duration of hospitalization may be potentially beneficial in decreasing the rate of infections. Interventional studies are needed to address these issues.

Although evidence has shown that stigma can impair patients' psychological health, few studies have addressed stigma and its relation to psychosocial status in CHBV patients. Investigating stigma in more depth and with respect to diverse psychological and sociocultural backgrounds may help health care system in improving quality of care among CHBV patients.

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