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Prevalence of Major Depression and Its Associations With Demographic and Clinical Characteristics and Quality of Life in Chinese Patients With HBV-related Liver Diseases

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ABSTRACT

BACKGROUND: There are no data about the frequency of major depression in patients with liver disease related to Hepatitis B virus (HBV) in China. This study examined the prevalence of major depression and its clinical correlates and association with quality of life (QOL) in patients with HBV-related liver diseases.
METHOD: Altogether 634 patients with HBV-related liver diseases met study entry criteria and completed the survey. The diagnosis of major depression was established with the Mini International Neuropsychiatric Interview (MINI). Socio-demographic and clinical characteristics, Global Assessment of Functioning (GAF) and QOL were measured.
RESULTS: The prevalence of major depression was 6.4%. Multivariable logistic regression analyses revealed that insomnia ($P = 0.01$, OR = 5.5, 95%CI = 1.4–21.6) and global functioning ($P < 0.001$, OR = 0.6, 95% CI = 0.5–0.7) were independently associated with major depression. Major depression was associated with both poor physical ($F_{(1, 634)} = 4.0$, $P = 0.04$) and mental QOL ($F_{(1, 634)} = 26.2$, $P < 0.001$).
CONCLUSIONS: Given the negative impact of depression on patients' QOL, more attempts should be made to identify and treat it in HBV-related diseases.

INTRODUCTION

Hepatitis B virus (HBV) infection is a prevalent infectious disease (Shepard, Simard, Finelli, Fiore, & Bell, 2006). The World Health Organization estimated that approximately 2 billion people have serologic evidence of present or past HBV infection and 350–400 million people are chronically infected (Custer et al., 2004; MacLachlan, Locarnini, & Cowie, 2015; WHO, 2016). In China, there are around 93 million HBV carriers and about 30 million suffer from chronic hepatitis B (Liang et al., 2009). Hepatitis B infection is highly contagious and greatly increases the risk of chronic hepatitis, hepatic cirrhosis and hepatocellular carcinoma (HCC) (Chan, Wong, Qin, & Chan, 2016). HBV-related diseases cause immeasurable suffering for patients and their families and enormous economic and social costs. For example, more than one billion USD per year is spent on diseases related to hepatitis B infection in the USA (Keshavarz et al., 2015).

HBV-related diseases are associated with fatigue, loss of appetite, abdominal pain and psychological disturbances, such as low self-esteem (Gutteling et al., 2006; Kim, Oh, & Lee, 2006). In addition, discrimination and stigma related to HBV disease often affect patients and their families (Huang et al., 2016; Kan, Wen, & Xue, 2015). Patients with HBV-related diseases are prone to suffer from loneliness, hopelessness and social isolation (Gutteling, de Man, Busschbach, & Darlington, 2007; Gutteling et al., 2006). All these factors could increase the risk of psychiatric comorbidities, particularly depression (Mirabdolhagh, Dormohammadi, Nasiri, Tavakoli, & Shahbazi, 2015).

A few studies examined the prevalence of depression in HBV-infected patients in China. Duan et al. (Duan, Kong, Zhang, & Guo, 2012) examined 120 patients with HBV-infection using the Hamilton Depression Rating Scale (HAMD) and found that compared to the healthy controls, patients had significantly higher levels of depression. Zhu et al. (Zhu et al., 2016) measured depressive symptoms with the HAMD in 114 patients with chronic hepatitis B (CHB) and cirrhosis and found that

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depressive symptoms in liver cirrhosis were associated with the severity of cirrhosis. The common limitation of these studies was the small sample size, which limits generalizability and precision. In addition, the diagnosis of depressive illness was inadequate as it was based only on simple questionnaires instead of thorough psychiatric assessment.

The aim of this study was to examine the point prevalence (prevalence thereafter) of major depression using a structured clinical interview, the Mini International Neuropsychiatric Interview (MINI (Sheehan et al., 1998; Si et al., 2009)) and its associations with demographic and clinical characteristics and quality of life (QOL).

METHODS

STUDY SETTING AND PATIENTS

This study was conducted between June 1, 2014 and January 31, 2015 in Beijing YouAn Hospital, an 800-bed university-affiliated teaching hospital for infectious diseases. In- and out-patients were consecutively screened and recruited if they were (1) 18 years or above; (2) diagnosed as being a HBV carrier, or having CHB, hepatitis B cirrhosis or HCC according to the Guidelines of Prevention and Treatment for Chronic Hepatitis B (Jia & Li, 2011) and the Recommendations of the Asian Pacific Association for the Study of the Liver (APASL) for the management of hepatocellular carcinoma (Sarin et al., 2009); (3) of Chinese descent; (4) able to communicate, tolerate the one-hour interview, and understood the purpose of the study. Patients who had major depression before the diagnosis of HBV infection were excluded. The study protocol was approved by the Beijing YouAn Hospital Clinical Research Ethics committee. All patients provided written informed consent.

ASSESSMENT INSTRUMENTS AND EVALUATION

Each patient was interviewed by one of two research physicians who were experts in HBV related illness and trained to conduct depression diagnostic screening. Socio-demographic data were collected using a data collection form designed for this study.

The diagnosis of major depression according to DSM-IV was established with the Chinese version of the MINI, Version 5.0 (Sheehan et al., 1998; Si et al., 2009). The 10-item Chinese version of the Montgomery-Asberg Depression Rating Scale (MADRS) was used to measure the severity of depressive symptoms within the past week (Montgomery & Asberg, 1979; Zhong, Wang, Chen, & Wang, 2011). QOL was measured with the Chinese version of the Medical Outcomes Study Short Form 12 (SF-12) (Jenkinson & Layte, 1997; Zhang et al., 2011). The SF-12 is a generic instrument with 12 items addressing eight health domains: physical functioning, role limitations due to physical problems, bodily pain, vitality, and social functioning as well as role limitations with each domain keyed to emotional or mental health problems. For the purpose of statistical analysis, the first four domains were collapsed into a physical component score, while the remaining four domains formed a mental component score. A higher score on SF-12 indicates better QOL.

The Global Assessment of Functioning (GAF) was used to evaluate overall psychosocial functioning (Startup, Jackson, & Bendix, 2002). Lower scores indicate poorer level of functioning. A person was regarded alcohol user if s/he drank at least one alcoholic beverage each month in the last year (Xiang et al., 2009). The presence of three basic forms of insomnia during the past month was ascertained (Liu & Zhou, 2002; Liu, Uchiyama, Okawa, & Kurita, 2000) by asking three questions: *"Do you have difficulties in falling sleep?"* for difficulty initiating sleep (DIS); *"Do you have the difficulties in maintaining sleep and wake up often?"* for difficulty maintaining sleep (DMS); and *"Do you wake up in the midnight or early morning and have difficulties in falling sleep again?"* for early morning awakening (EMA). Patients answering "often" to at least one of the three questions belonged to the "insomnia" group.

STATISTICAL ANALYSIS

Data were analyzed using SPSS 21.0 for Windows. Comparisons between patients diagnosed with major depression or not for demographic and clinical variables were performed using chi-square tests, *t*-tests and Mann-Whitney *U* test, as appropriate. QOL was compared between groups using analysis of covariance (ANCOVA) after controlling for the potentially confounding effects of variables that significantly differed in above univariate analyses. The independent associations of demographic and clinical characteristics with major depression were conducted by multivariable logistic regression analyses using the "Enter" method. Major depression was entered as the dependent variable, while variables age, gender, education, marital status, local residence, personal income, family history of psychiatric disorders, medical history, diagnoses of HBV-related liver diseases, age of onset of HBV, duration of HBV-related liver disease, current use of alcohol, insomnia, GAF scores and stigma score were entered as the independent variables. Due to collinearity between the site of treatment (in- or out-patient) and HBA diagnoses, age of onset of HBV and number of hospitalizations, treatment site and number of hospitalizations were not entered in the logistic regression model. The level of significance was set at 0.05 (two-tailed).

RESULT

Altogether 812 patients with chronic HBV infection were invited to participate in the study; 634 patients (454 men and 180 women) met the inclusion criteria and completed the assessment, yielding a 78.1% participation rate. Then proportions of HBV carrier, chronic hepatitis B, HBV-related cirrhosis, HBV-related HCC were 9.5%, 36.2%, 28.5% and 25.8%, respectively. The prevalence of major depression was 6.4%.

Table 1
Basic demographic and clinical characteristics of the sample (n = 634).

	HBV carrier (n = 60)		Chronic hepatitis B (n = 229)		HBV-related cirrhosis (n = 181)		HBV-related HCC (n = 164)	
	N	%	N	%	N	%	N	%
Inpatients	0	0	0	0	181	100.0	164	**100.0**
Male gender	33	55.0	149	65.1	139	76.8	131	**79.9**
Married	47	78.3	188	82.1	166	91.7	149	**90.9**
Local resident	27	45.0	76	33.2	77	42.5	92	**56.1**
Living alone	2	3.3	6	2.6	9	5.0	5	**3.0**
Personal income <3000 yuan	15	25.0	54	23.6	69	38.1	72	**43.9**
Having health insurance	0	0	4	1.7	7	3.9	3	**1.8**
Family history of psychiatric disorders	2	3.3	8	3.5	2	1.1	5	**3.0**
Current alcohol use	15	25.0	43	18.8	30	16.6	21	**12.8**
History of medical conditions	21	35.0	72	31.4	83	45.9	106	**64.6**
Insomnia	14	23.3	52	22.7	45	24.9	55	**33.5**
Major depression	4	6.7	16	7.0	11	6.1	10	**6.1**
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Age (years)	37.1	11.8	39.2	12.1	52.2	10.9	**58.4**	8.5
Age of onset of HBV (years)	26.7	14.7	28.5	12.5	36.8	14.0	**40.2**	13.2
Duration of HBV-related liver disease (years)	11.8	9.0	10.9	9.5	15.6	12.5	**17.5**	11.4
Education (years)	11.8	4.0	11.4	3.6	10.4	5.1	**10.9**	5.0
GAF total	75.7	13.7	75.8	12.5	74.5	12.8	**72.1**	11.8
MADRS	6.0	8.6	5.2	6.5	6.8	7.2	**8.2**	7.5
SF-12 physical	51.0	5.8	49.4	6.8	64.8	16.2	**65.8**	14.0
SF-12 mental	50.5	9.4	51.1	10.5	55.6	16.4	**54.0**	15.7

Bolded values are $p < 0.05$; Chronic HBV-Infection Related Stigma Scale = HIRSS; GAF = Global Assessment of Functioning; HCC = hepatocellular carcinoma; HAMA = Hamilton Anxiety Rating Scale; MADRS = Montgomery-Asberg Depression Rating Scale; SF-12 = Medical Outcomes Study Short Form 12.

Table 1 shows the basic demographic and clinical characteristics of patients by HBV-related liver diseases. Table 2 presents the demographic and clinical characteristics of the entire sample and separately by major depression. After controlling for confounders, there were significant differences between the major depression and no-major depression groups in physical ($F_{(1, 634)} = 4.0$, $P = 0.04$) and mental ($F_{(1, 634)} = 26.2$, $P < 0.001$) QOL domains. Multivariable logistic regression analyses revealed that insomnia ($P = 0.01$, OR = 5.5, 95% CI = 1.4–21.6) and global functioning ($P < 0.001$, OR = 0.6, 95% CI = 0.5–0.7) were independently associated with major depression (Table 3).

DISCUSSION

This was the first study that examined the prevalence of major depression, its correlates and QOL utilizing a clinical interview and standardized diagnostic tools in patients with HBV-related liver diseases in China.

In this study, the prevalence of major depression was considerably lower than the figures reported among patients with HBV-related liver diseases from other parts of the world, such as 19.8% in Iran, 58.6% in Pakistan and 14.0% in Turkey (Atesci, Cetin, Oguzhanoglu, Karadag, & Turgut, 2005; Mirabdolhagh et al., 2015; Qureshi, Khokhar, & Shafqat, 2012). The discrepancy across studies may be partly due to the difference in severity of HBV-related liver diseases and measurement instruments. In this study the prevalence of major depression was significantly higher than in the Chinese general population (1.6%) (Gu et al., 2013). There are several possible reasons for the higher prevalence of major depression. HBV-related diseases are accompanied with somatic complaints, such as fatigue, and muscle cramps, which may increase the risk of depression (Kim et al., 2006; Yilmaz et al., 2016). In addition, due to the infectious nature of HBV, discrimination against people with HBV-related liver diseases remains widespread in China (Huang et al., 2016; Kan et al., 2015). People with HBV-related diseases often face social isolation, a contributing factor to the development of depression (Atesci et al., 2005). Furthermore, depression is one of the side effects of interferon given against HBV infection (Arslan, Buyukgebiz, Ozturk, & Akay, 2003; Hunt et al., 1997; Keskin, Gumus, & Orgun, 2013). Finally, in China, patients with HBV-related diseases and their families are often stigmatized (Huang et al., 2016; Kan et al., 2015), and families have to cope with discrimination and shame. In an attempt to maintain the families' honor, the patient conceals or denies their infectious disease status, a phenomenon called 'courtesy stigma' (Goffman, 1968). Such familial "courtesy stigma" is thought to increase the risk of depression (Yue et al., 2013; Zhuang et al., 2014).

Female gender and socioeconomic status have been found to be significantly associated with depression in the Chinese general population and some special populations, such as migrant workers (Ma et al., 2009; Zhong et al., 2015). This study could not confirm these associations. The possible reason may be that in this population the association of depression with gender and socioeconomic status was mediated by disease-relate variables, such as severity of HBV-related liver diseases and side effects of interferon therapy (Kovacs, Kovacs, Eszlari, Gonda, & Juhasz, 2016).

Depression was reported to be one of the strongest predictors of QOL (Xiang, Weng, Leung, Tang, & Ungvari, 2008), which was confirmed in this study. Similar to previous findings (Atesci et al., 2005; Enescu, Mitrut, Balasoiu, Turculeanu, & Enescu, 2014; Kunkel et al., 2000), depression was associated with lower QOL and impaired global functioning, which may be due to obstacles to social integration and impaired occupational functioning associated with HBV infection. In this study, insomnia was positively associated with depression. This was expected as insomnia is one of the diagnostic criteria of major depression (American Psychiatric Association, 1994). Depression is associated

Table 2
Demographic and clinical characteristics of the whole sample and separately by major depression.

	Total sample (n = 634)		No major depression (n = 593)		Major depression (n = 41)		Statistics		
	N	%	N	%	N	%	χ^2	df	p
Inpatients	345	54.4	324	54.6	21	51.2	0.1	1	0.6
Male sex	454	71.6	430	72.5	22	53.7	6.6	1	**0.01**
Married	550	86.8	514	86.7	36	87.8	0.04	1	0.8
Local residents	272	42.9	260	43.8	12	29.3	3.3	1	0.06
Living alone	22	3.5	20	3.4	2	4.9	0.005	1	0.9
Personal income <3000 yuan	210	33.1	194	32.7	16	39.0	0.6	1	0.4
Having health insurance	14	2.2	13	2.2	1	2.4	0.01	1	0.9
Family history of psychiatric disorders	17	2.7	14	2.4	3	7.3	1.9	1	0.1
Current alcohol use	109	17.2	103	17.4	6	14.6	0.2	1	0.6
History of medical conditions	282	44.5	262	44.2	20	48.8	0.3	1	0.5
HBV-related liver disease							0.1	3	0.9
Carrier	60	9.5	56	9.4	4	9.8			
CHB	229	36.1	213	35.9	16	39.0			
Cirrhosis	181	28.5	170	28.7	11	26.8			
HCC	164	25.9	154	26.0	10	24.4			
Insomnia	166	26.2	133	22.4	33	80.5	66.8	1	<**0.001**
	Mean	SD	Mean	SD	Mean	SD	T / Z	df	p
Age (years)	48.0	13.8	47.9	13.9	44.7	12.1	1.4	632	0.2
Age of onset of HBV (years)	34.1	14.6	34.0	14.3	29.9	13.4	1.7	632	0.6
Duration of HBV-related liver disease (years)	14.0	11.4	13.9	11.0	15.5	14.4	−0.8	–[a]	0.3
Education (years)	11.2	4.8	11.1	4.6	9.9	3.7	1.6	632	0.5
GAF	74.5	12.6	76.0	11.4	52.3	6.4	13.0	632	<**0.001**
SF-12 physical	46.2	8.2	46.4	7.9	43.1	11.6	2.4	632	<**0.001**
SF-12 mental	49.1	10.1	50.4	8.8	30.6	9.7	13.6	632	0.3

[a] = Mann-Whitney *U* test; bolded values are $p < 0.05$; CHB = chronic hepatitis B; GAF = Global Assessment of Functioning; HCC = hepatocellular carcinoma; MADRS = Montgomery-Asberg Depression Rating Scale; MINI = Mini International Neuropsychiatric Interview; SF-12 = Medical Outcomes Study Short Form 12.

Table 3
Socio-demographic and clinical correlates of major depression (logistic regression analysis).

	Major depression		
	p	OR	95% CI
Male sex	0.2	2.7	0.4–15.7
Married	0.8	0.8	0.1–4.8
Local resident	0.3	2.0	0.5–8.4
Personal income <3000 yuan	0.3	1.9	0.4–8.3
Family history of psychiatric disorders	0.3	3.1	0.3–31.1
Current alcohol use	0.8	1.2	0.2–6.4
History medical conditions	0.3	0.4	0.1–2.0
HBV-related liver disease			
Carrier		1.0	
CHB	0.2	5.6	0.3–102.5
Cirrhosis	0.8	1.4	0.06–32.9
HCC	0.8	1.3	0.04–41.9
Insomnia	**0.01**	**5.5**	**1.4–21.6**
Age	0.8	0.9	0.8–1.1
Education (years)	0.06	0.8	0.6–1.01
Age of onset of HBV (years)	0.9	0.9	0.8–1.1
Duration of HBV-related liver disease (years)	0.7	1.03	0.8–1.2
GAF total	<**0.001**	**0.6**	**0.5–0.7**

Bolded values are $p < 0.05$; Chronic HBV-Infection Related Stigma Scale = HIRSS; GAF = Global Assessment of Functioning; CHB = Chronic Hepatitis B; HCC = hepatocellular carcinoma; MADRS = Montgomery-Asberg Depression Scale; MINI = Mini International Neuropsychiatric Interview.

with lack of energy, difficulties concentration and fatigue (Irwin, 2001), which may lead to daytime naps thereby increasing the risk of insomnia at night.

The strengths of this study include the large, consecutively selected and homogeneous sample and the use of physician administered standardized clinical interviews to diagnosis major depression. However, the results should be interpreted with caution due to several limitations. First, due to the cross-sectional design, the causality between depression and its correlates could not be identified. Second, insomnia was evaluated only by self-report, thus recall bias could not be excluded. Finally, some important variables, such as family support, have not been examined.

In conclusion, a high burden of depression was found and associated with poor patient physical and mental health QOL. Surveillance and treatment of depression among patients with HBV-related diseases should become a priority.

CONFLICT OF INTEREST

The authors report no conflict of interest in conducting this study and preparing the manuscript.

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