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Family history of liver cancer may indicate chronic hepatitis B virus infection in an endemic area

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ABSTRACT

Objective: To find additional factors suggestive of hepatitis B virus (HBV) infection in the general population.
Methods: This study collected data on HBV infection from the hepatitis virus survey. The survey was conducted in 13 provinces in the Northeastern Thailand in 2014 and 2015. During the survey, HBV screening was performed by using blood test. A questionnaire was also distributed to all participants for collection of baseline data on characteristics, risk factors for HBV infection, and daily life activities.
Results: There were 2 008 participants involved in the survey. A total of 256 participants (12.75%) were tested positive for HBV infection. Only two factors were significantly associated with HBV infection, namely, male gender and family history of liver cancer. The adjusted ORs of both factors were 4.31 (95% *CI*: 2.28–8.12) and 2.26 (95% *CI*: 1.07–4.76), respectively.
Conclusions: Males in endemic areas with a family history of liver cancer should get tested for HBV as early as possible in order to detect chronic HBV infection regardless of whether they display symptoms of HBV infection or not.

1. Introduction

Chronic hepatitis B virus (HBV) infection is endemic in Southeast Asia, China, and Africa[1]. Its prevalence rate may be as high as 7%–8%[2]. In Thai HIV-1 infected pregnant women, the prevalence of HBV infection was 7.2%[3]. After a universal HBV vaccination campaign in Thailand, which began in 1992, the carrier rate has been decreased to 3.48% of general population[1]. Even though the carrier rate has been decreasing, HBV is still a significant risk factor for cirrhosis and hepatocellular carcinoma in the pre-vaccination era population.

Chronic HBV infection is a leading cause of hepatocellular carcinoma worldwide. HBV increases the risk of hepatocellular carcinoma by 1 000 times and is considered a cause of at least 50% of cases of hepatocellular carcinoma[4-7]. In Thailand, the estimated age-standardized incidence rate for liver cancer is 40.6 per 100 000 in men[8]. These cases are most commonly caused by HBV infection (73.6%)[9]. The under-recognition of hepatitis B infection and poor adherence to surveillance program in those diagnosed with hepatitis B result in high prevalence rates[10,11]. Most HBV carriers remain asymptomatic. The average age of HBV carriers at diagnosis was 30.9 years[8]. Risk factors for HBV infection may be different among countries and specific populations. Although there have been no identified risk factors found for HBV infection in blood donors in China[12], among Thai health care workers, being male, having a past history of jaundice, or having a family history of hepatocellular carcinoma are

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The study protocol was performed according to the Helsinki Declaration and approved by the Ethics Committee of the Faculty of Medicine, Khon Kaen University.
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significant risk factors for HBV infection[13]. This study aimed to find additional factors suggestive of HBV infection in the general population. Early detection and treatment may reduce the risk of cirrhosis and hepatocellular carcinoma.

2. Materials and methods

This study collected data on HBV infection from the hepatitis virus survey. The survey was conducted in 13 provinces in the Northeastern Thailand in 2014 and 2015. During the survey, HBV screening was performed by using blood test. The questionnaire was also distributed to all participants for collection of baseline data on characteristics, risk factors for HBV infection, and daily life activities. The study protocol was performed according to the Helsinki Declaration and approved by the Ethics Committee of the Faculty of Medicine, Khon Kaen University. Informed written consent was not obtained due to retrospective data collection.

Details of the questionnaire were as follows. Participants were asked about family history of liver cancer, history of HBV vaccination over their lifetime, alcohol consumption, smoking habits, herb/supplement use, and exercise habits. Family history of liver cancer was defined by the history of liver cancer in first-degree relatives. Alcohol consumption was categorized as 1) never and 2) used to or currently consumed. Similarly, smoking history was defined as current/previous smoker versus non-smoker. Exercise activities were categorized as whether or not the participant engaged in regular exercise for more than 30 min/day, three times a week.

Participants were divided into two groups according to the HBV test: HBsAg positive and negative. Data were compared between the groups using descriptive statistics. Univariate logistic regression analysis was applied to calculate the crude odds ratios (ORs) of individual variables for HBV infection. All variables were included in subsequent multivariate logistic regression analyses. A backward stepwise method was used to find the final model. Factors with *P* value of more than 0.25 were excluded. Analytical results were presented as adjusted ORs and 95% confidence interval (*CI*). All analyses were performed using STATA software (College Station, Texas, USA).

3. Results

There were 2 008 participants for the survey. Of those, 256 participants (12.75%) were tested positive for HBV infection. There were six significant factors that differed between those with and without HBV infection including age, sex, family history of liver cancer, alcohol consumption, history of smoking, and history of supplement/herb use (Table 1). Those with HBV infection had significantly lower mean age (46.03 *v.s.* 48.58 years) and lower proportion of supplement/herb use (27.75% *v.s.* 36.65%) than those without HBV infection. The HBV infection group had higher proportions than the non-HBV infection group in other categories. For example, family history of liver cancer was 27.40% in the HBV infection group and it was only 11.19% in the non-HBV infection group ($P < 0.001$).

Table 1
Baseline characteristics of subjects with and without HBV infection [*n* (%)].

Factors		Without HBV (*n* = 1752)	With HBV (*n* = 256)	*P* value
Gender	Female	1 257 (68.06)	127 (47.92)	< 0.001
	Male	590 (31.94)	138 (52.08)	
Mean age ± SD (years)		48.58 ± 14.63	46.03 ± 12.28	< 0.001
Body mass index (kg/m^2)	< 29	157 (8.80)	15 (5.84)	0.110
	> 29	1 627 (91.20)	242 (94.16)	
Family history of liver cancer	No	1 436 (88.81)	159 (72.60)	< 0.001
	Yes	181 (11.19)	60 (27.40)	
History of HBV vaccination	No	1 472 (86.44)	199 (84.32)	0.378
	Yes	231 (13.56)	37 (15.68)	
History of alcohol consumption	No	1 061 (64.34)	54 (47.79)	< 0.001
	Yes/used to	588 (35.66)	59 (52.21)	
Smoking history	No	1 426 (84.03)	163 (69.66)	< 0.001
	Yes/ex-smokers	271 (15.97)	71 (30.34)	
Supplement or herb use	No	1 020 (63.35)	164 (72.25)	0.009
	Yes	590 (36.65)	63 (27.75)	
Exercise	No	1 070 (63.09)	88 (71.54)	0.060
	Yes	626 (36.91)	35 (28.46)	

After adjustment by multivariate logistic regression, the final model was comprised of four factors (Table 2). Only two factors were significantly associated with HBV infection, namely, male gender and family history of liver cancer. The adjusted ORs of both factors were 4.31 (95% *CI*: 2.28–8.12) and 2.26 (95% *CI*: 1.07–4.76), respectively.

Table 2
Univariate and multivariate logistic regression analyses of factors associated with HBV infection.

Factors	Unadjusted odds ratio (95% *CI*)	Adjusted odds ratio (95% *CI*)
Male gender	2.31 (1.78–3.00)	4.31 (2.28–8.12)
Family history of liver cancer	2.99 (2.14–4.18)	2.26 (1.07–4.76)
Exercise	0.67 (0.45–1.01)	0.85 (0.72–1.01)
Supplement/herb use	0.66 (0.48–0.90)	0.66 (0.33–1.32)

4. Discussion

The prevalence of HBV infection in this study was 12.75%, which is higher than that in earlier reports[1,8]. There are two main reasons for this difference. First, the participants in this survey may be at higher-than-normal risk for HBV infection and, second, the average age was 46–48 years, indicating that they were not vaccinated in the universal HBV vaccination program.

The two main predictors for HBV infection are male gender and family history of liver cancer. According to a CDC report, 30% of HBV infections occur in the adulthood[14]. Similar to HIV infection, male is at higher risk than female. The results of this study may suggest that participants were infected with

HBV as adults, as both genders are at equal risk for perinatal and childhood HBV infection. Family history of liver cancer is another independent predictor for HBV infection.

Perinatal and childhood transmission leads to chronic HBV infection at a rate of 95% and 50%, respectively[8], which results in a higher risk for hepatocellular carcinoma in family members. A study from China also found that family history of liver cancer was a significant risk factor for hepatocellular carcinoma with an odds ratio of 2.241[15]. It was noted that supplement/herb use was shown to be another significant factor using univariate logistic analysis. However, after being adjusted for other factors, it was no longer a significant factor (Table 2). We, therefore, would like to recommend that in endemic areas, males with a family history of liver cancer should get tested for HBV as early as possible in order to detect chronic HBV infection, particularly in countries where resources are limited.

There are several limitations to this study. First, although this study included participants from almost every province in the Northeast Thailand, it may not be representative of the general population in the northeast or Thailand as a whole. Second, some other factors are not included in the study such as the presence of fatty liver disease, cholesterol levels, or HBV genotypes. However, body mass index, smoking, and alcohol consumption were not independent factors for HBV infection in our results. Third, the results of this study may not be universal, particularly for areas that are not endemic for HBV infection. Further studies are needed to confirm the results of this study, both in endemic and non-endemic countries.

Male gender and family history of liver cancer are predictors of HBV infection in endemic areas. Males with a family history of liver cancer should get tested for HBV as early as possible, in order to detect chronic HBV infection regardless of whether they display symptoms of HBV infection or not.

Conflict of interest statement

We declare that we have no conflict of interest.

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