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Who should be checked for hepatitis C virus infection in endemic areas?

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ABSTRACT

Objective: To find additional factors suggestive of hepatitis C virus (HCV) infection in the general population by using data from a hepatitis virus survey.

Methods: This study collected data of HCV infection from a hepatitis virus survey. The survey was conducted in 13 provinces in the northeast Thailand in 2014 and 2015. During the survey, a blood test was performed to screen for HCV. A questionnaire was also distributed to all participants asking about baseline characteristics, risk factors for HCV infection, and daily life activities. Risk factors for HCV infection were executed.

Results: There were 2112 participants for the survey. Of those, 110 participants (5.21%) tested positive for HCV infection. After adjustment by multivariate logistic regression, three factors were significantly associated with HCV infection, namely male gender, age, and family history of liver cancer. The adjusted *OR*s and 95% *CI* of these factors were 3.14 (1.50, 6.56), 3.78 (1.12, 12.76), and 2.28 (1.08, 4.80), respectively.

Conclusions: Male gender, increasing age, and family history of liver cancer are predictors of HCV infection in endemic areas. Males with a family history of liver cancer in their first-degree relatives should be tested for HCV infection regardless of symptoms.

1. Introduction

Chronic hepatitis C virus (HCV) is an emerging infection worldwide. The HCV infection rate increased globally from 2.3% in 1990 to 2.8% in 2005 [1]. In that year, there were an estimated of 185 million people suffering from HCV infection, which may cause more than 350000 deaths annually [1,2]. The HCV prevalence rate varies among countries. It is more prevalent in developing countries such as those in East Asia or Southeast Asia. Similar to HBV, HCV is a cause of both cirrhosis and hepatocellular carcinoma. Approximately one-fourth of cirrhosis or hepatocellular carcinoma cases are caused by HCV [2]. In Japan, HCV was highly associated with hepatocellular carcinoma at 90% [2].

Unlike HBV infection, there is no effective vaccine against HCV and most people infected with HCV develop chronic HCV infections (80%) [3]. HCV seems to be more problematic for public health than HBV. Additionally, people infected with chronic HCV may remain asymptomatic for years before development of cirrhosis and hepatocellular carcinoma [4]. People may not be aware of this kind of HCV infection, particularly in developing countries where people are not well informed about health matters. HCV is mainly transmitted to humans via blood components. In Thailand, the main risk factors for HCV infection among blood donors are intravenous drug use or history of blood transfusion [5]. This

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study aimed to find additional factors suggestive of HCV infection in the general population by using data from a hepatitis virus survey. Early detection and treatment may reduce risk of cirrhosis and hepatocellular carcinoma. Additionally, these data may apply to populations in other Asian countries.

2. Materials and methods

This study collected data of HCV infection from a hepatitis virus survey. The survey was conducted in 13 provinces in the northeastern Thailand in 2014 and 2015. Each survey was announced via local media such as radio or advertisement. Persons who registered in advance and participated in the program were enrolled in the study. During the survey, a blood test was performed to screen for HCV. A questionnaire was also distributed to all participants asking about baseline characteristics, risk factors for HCV infection, and daily life activities.

Details of the questionnaire were as follows. Participants were asked about family history of liver cancer, history of HBV vaccination over their lifetimes, 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. History of HBV vaccination in their lifetime was asked. Alcohol consumption was categorized as 1) never 2) used to or currently consumed. Similarly, smoking history was defined as current/previous smoker *vs*. non-smoker. History of current supplements/herb use was asked. Exercise activities were categorized as whether or not the participant engaged in regular exercise for more than 30 min/d three times a week.

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

3. Results

There were 2 112 participants for the survey. Of those, 110 participants (5.21%) tested positive for HCV infection. There were six significant factors between those with and without HCV infection including age, sex, family history of liver cancer, alcohol consumption, history of smoking, and history supplement/herb use (Table 1). Those with HCV infection had significantly higher mean age (50 *vs*. 48 years; $P < 0.001$) and lower proportion of supplement/herb use (25% *vs*. 36%; $P = 0.034$) than those without HCV infection. The HCV infection group had higher proportions than the non-HCV infection group in other categories. For example, the HCV infection group had a higher proportion of males than non-HCV infection group (63% *vs*. 32%; $P < 0.001$).

After adjustment by multivariate logistic regression, the final model comprised of six factors (Table 2). Only three factors were significantly associated with HCV infection, namely male gender, age, and family history of liver cancer. The adjusted *OR*s and 95% *CI* of these factors were 3.14 (1.50, 6.56), 3.78 (1.12, 12.76), and 2.28 (1.08, 4.80), respectively.

Table 1
Baseline characteristics of subjects with and without HCV infection.

Factors	Non-HCV (n = 2002)	HCV (n = 110)	P value
Gender			<0.001
Female	1344 (67.13)	40 (36.36)	
Male	658 (32.87)	70 (63.64)	
Mean age (years)	48.13 (14.59)	50.64 (9.65)	<0.001
Body mass index (kg/m^2)			0.278
<29	160 (8.27)	12 (11.21)	
>29	1774 (91.73)	95 (88.79)	
Family history of liver cancer			0.032
No	1526 (87.25)	69 (79.31)	
Yes	223 (12.75)	18 (20.69)	
History of HBV vaccination			0.761
No	1589 (86.12)	82 (87.23)	
Yes	256 (13.28)	12 (12.77)	
Alcohol consumption			0.023
Never	1082 (63.80)	33 (50.00)	
Currently/used to	614 (36.20)	33 (50.00)	
Smoking history			<0.001
Never	1529 (83.46)	60 (60.61)	
Currently/used to	303 (16.54)	39 (39.39)	
Supplements/herb use			0.034
No	1118 (63.92)	66 (75.00)	
Yes	631 (36.08)	22 (25.00)	
Exercise			0.589
No	1110 (63.54)	48 (66.67)	
Yes	637 (36.46)	24 (33.33)	

Table 2
Univariate and multivariate logistic regression analysis of factors associated with HCV infection.

Factors	Unadjusted *OR* (95% *CI*)	Adjusted *OR* (95% *CI*)
Male gender	3.57 (2.39, 5.32)	3.14 (1.50, 6.56)
Age (year)	6.05 (2.21, 16.53)	3.78 (1.12, 12.76)
Family history of liver cancer	1.78 (1.04, 3.05)	2.28 (1.08, 4.80)
Body mass index (kg/m^2)	0.71 (0.38, 1.32)	0.50 (0.16, 1.55)
Supplement/herb use	0.59 (0.36, 0.96)	0.59 (0.30, 1.17)
Smoking history	3.28 (2.15, 4.99)	2.03 (0.99, 4.13)

4. Discussion

The prevalence of HCV infection in this study was 5.21%, which is higher than that in other reports and in the general population [6,7]. The estimated prevalence of HCV infection in the published literature was 2.7% [6], while another report from Thailand showed the prevalence of HCV infection to be 0.94% [7]. The reason for low prevalence rate of the latter report was that blood samples were collected primarily from pediatric health checkups. The mean age of the participants was quite young, resulting in a low rate of HCV infection. Further extensive studies should be conducted to confirm the national HCV infection rate in Thailand. The high HCV infection rate in this study may be due to two factors. First, participants in the survey may be at higher-than-normal risk for HCV infection; second,

participants had an average age of 48–50 years, which meant that they were at higher risk than younger people.

There are three independent factors associated with HCV infection, including male gender, age, and family history of liver cancer. These results suggested that males with a family history of liver cancer in their first-degree relatives should be tested for HCV infection, regardless of symptoms. For every one-year increase in age, risk of being found to be HCV positive increased by 3.78 times. This recommendation may apply to endemic countries for HCV infection, particularly developing countries [8].

There are two explanations for why men had a higher risk for HCV infection than women. These are gender risk and HCV clearance ability. HCV is primarily transmitted by through blood, putting intravenous drug users, tattoo recipients, and men who engage in sexual intercourse with other men particularly at risk [9–11]. Men are at higher risk of contracting an infection in these ways than are women. A report from Egypt [12] found that females also had a higher ability to clear the HCV virus than men (44.6% *vs*. 33.7%; P = 0.001). Increased age is also associated with increased risk for HCV infection. A systematic review found that three out of six articles indicated that age was an independent factor for HCV infection [13]. A recent study from China also found that the most common age group was between 41 and 60 years and accounted for 60% of all HCV infected patients [14].

A family history of liver cancer increases the risk for HCV infection by 2.28 times. This finding may indicate that HCV may be transmitted among family members, vertically or other routes. Theoretically, the rate of HCV vertical transmission is much lower than HBV [15,16]. The transmission rate is 70%–90% for HBe positive and 10%–40% for HBs positive HBV pregnant carriers [15], while HCV transmission rate is 3%–10% [16]. HCV may spread to spouse for five times in HCV group than non-HCV group (*OR* = 5.75, 95% *CI*: 1.94–17.07) [14]. Parents with the HCV gene have also been reported to pass HCV to their children via sperm [17]. This evidence suggests that it is possible that HCV may be vertically transmitted or transmitted among family members and cause liver cancer in families. Those people with a family history of liver cancer, HBV or HCV should be tested. A study from China [14] also indicated that a family history of HCV infection is associated with HCV infection with adjusted odds ratio of 4.68 (95% *CI* of 2.67, 8.75). It may, therefore, be worthwhile to screen for HCV infection in patients with a family history of HCV infection. Other routes of transmission such as oral route as in *Campylobacter pylori* require further investigation.

There are several limitations to this study. First, although it 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, history of tattooing, or HCV genotypes. Body mass index, smoking, and alcohol consumption were included in the analysis, but they were not independent factors for HCV 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.

In conclusion, male gender, increasing age, and family history of liver cancer are predictors of HCV infection in endemic areas. Males with a family history of liver cancer in their first-degree relatives should be tested for HCV infection regardless of symptoms. Early HCV screening in younger age groups is more beneficial than HCV.

Conflict of interest statement

We declare that we have no conflict of interest.

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