Factors Associated with Awareness of Infection Status among Chronic Hepatitis B and C Carriers in Korea

Aesun Shin,[1] Eo Rin Cho,[1] Jeongseon Kim,[1] Joohon Sung,[5] Kyung Woo Park,[2] Min-Kyung Lim,[3] and Hai-Rim Shin[4,6]

[1]Cancer Epidemiology Branch, Division of Cancer Epidemiology and Management, Research Institute, National Cancer Center; [2]Center for Early Detection and Prevention, National Cancer Center Hospital, National Cancer Center; [3]National Cancer Information Center and [4]Cancer Registration and Statistics Branch, National Cancer Control Institute, National Cancer Center, Goyang-si, Gyeonggi-do, South Korea; [5]The Graduate School of Public Health and Institute of Health and Environment, Seoul National University, Seoul, South Korea; and [6]International Agency for Research on Cancer, Lyon, France

Abstract

Hepatitis B (HBV) and hepatitis C (HCV) viral infections are the most important risk factors for hepatocellular carcinoma (HCC), which is responsible for 17.5% of cancer deaths in Korea. The objectives of this study were to identify demographic characteristics that may affect hepatitis carriers' awareness of their infection status, and to assess whether health-related behaviors differed by awareness of the infection. Among 18,636 persons who were recruited from a cancer screenee cohort, 904 were HBV carriers and 146 were HCV carriers. Among the HBV carriers, 74.2% were aware of their infection status. Higher education (odds ratio, 1.8; college versus middle school or less), family history of liver cancer or disease, and marriage were associated with awareness of HBV infection status. Participants who were aware of their HBV carrier status were more likely to be former smokers or drinkers than those who were not aware of their status. Only 34.9% of HCV carriers were aware of their HCV infection status. No demographic characteristics were related to awareness of HCV infection status among HCV carriers. However, HCV carriers who were aware of their infection status were more likely to be former drinkers (odds ratio, 9.2; 95% confidence interval, 1.8-47.2). In conclusion, two thirds of HCV carriers and one fourth of HBV carriers in this study population were not aware of their infection status, and awareness of hepatitis infection status was significantly associated with other risk behaviors, such as alcohol consumption and cigarette smoking. (Cancer Epidemiol Biomarkers Prev 2009;18(6):1894–8)

Introduction

Hepatitis B (HBV) and hepatitis C (HCV) infections are the most important risk factors for hepatocellular carcinoma (HCC), which is responsible for 17.5% of cancer deaths in Korea. In 2007, 8,389 men and 2,755 women died from malignant neoplasms of the liver and intrahepatic bile ducts.[7] According to the Korea National Cancer Registry, 14,907 new liver cancer cases were reported in the year 2005.[8] Although the incidence of liver cancer has decreased by an average of 1.6% every year between 1999 and 2005, liver cancer contributes greatly to the overall disease burden as the third most frequent cancer in men and the seventh most frequent in women. Among malignant neoplasms, liver cancer held the highest value for expected years of life lost among men and the second highest value among women (1). Most HCCs develop in patients who have chronic liver disease or cirrhosis (2). The annual incidence of HCC among compensated cirrhosis patients was estimated between 1.4% and 3.3% (3-5). According to the third National Health and Nutrition Survey of Korea, the prevalence of hepatitis surface antigen was 4.2% among men and women ages 20 years and older (6). The prevalence was higher in men (4.9%) than women (3.4%), and the total number of HBV carriers was estimated to be ~1,500,000 persons in the year 2005 (6). Fortunately, the prevalence of HBV carriers has decreased from 5.1% in the year 1998 to 4.2% in the year 2005. The prevalence of HCV among Koreans ages 40 years and older was estimated at 1.39% from 1995 to 2000 and had declined from a prevalence of 2.9% from 1990 to 1994 (7).

The National Cancer Screening Program of the Ministry for Health, Welfare, and Family Affairs recommends screening for HCC using ultrasonography and serum α-fetoprotein every 6 months for those who are 40 years of age or older and who are HBV or HCV carriers or have liver cirrhosis.[9] Although the National Health Screening Program provided by the National Health Insurance Corporation (NHIC), which covers the entire South Korean population, measures anti-HBV antibody and HBV surface antigen, HBV carriers who have never participated in a health check-ups might not be aware of their hepatitis viral infection status. Moreover, because HCV screening is not a part of regular health check-ups provided by the NHIC, these high-risk groups may not recognize their infection status. If individuals are not aware

Received 12/21/08; revised 4/6/09; accepted 4/14/09; published OnlineFirst 5/19/09.

Grant support: The National Cancer Center (Korea) grant 0610552.

Requests for reprints: Aesun Shin, Cancer Epidemiology Branch, Division of Cancer Epidemiology and Management, National Cancer Center Research Institute, 111 Junbalsanro, Ilsandong-gu, Goyang-si, Gyeonggi-do 410-769, South Korea. Phone: 82-31-920-2571; Fax: 82-31-920-2579; E-mail: shina@ncc.re.kr

doi:10.1158/1055-9965.EPI-08-1228

[7] http://www.kosis.kr
[8] http://ncc.re.kr
[9] http://ncc.re.kr/english/programs/progarms03.jsp

of their hepatitis viral infection status, they will not receive appropriate cancer screenings.

The objectives of this study were to identify demographic characteristics associated with awareness of infection status among hepatitis carriers, and to assess whether health-related behaviors were different depending on a carrier's awareness of one's infection status.

Materials and Methods

Cancer Screening Program and Participants. The eligible study participants were age 30 y or above and were enrolled through the cancer screening program at the National Cancer Center (NCC) in South Korea. The cancer screening program at NCC is a multiphase program that encompasses routine health examinations, screening for selected cancers, and a self-report questionnaire. The NCC health examination center organizes several different cancer screening program packages, and the examinee is responsible for the health examination fee. Routine check-ups consist of blood chemistries, lipid battery, fasting glucose and insulin levels, chest X-ray, eye examination, routine urine and stool examinations, etc. Stomach (gastrofibroscopy), colon (colonoscopy), breast (mammography), uterine cervix (Pap smear), liver (ultrasonography and serum α-fetoprotein), and prostate (serum prostate specific antigen) are the typical target sites and methods for cancer screenings. A total of 18,636 subjects provided written informed consent for study participation between August 2002 and August 2008. Among them, 10,327 (55.4%) were male.

Measurements. Serologic tests for viral hepatitis infection status are one of the routine check-up items. HBV surface antigen and HCV antibody were measured in serum by chemiluminescent immunoassay (ARCHITECT i2000, Abbott Laboratories). The self-administered questionnaire included a range of standardized tools measuring lifestyle and health behavior, such as family history and medical history of cancers and other chronic disease, cigarette smoking and alcohol consumption, regular exercise, dietary habits, socioeconomic status, and demographic characteristics. The awareness for viral infection status was determined by self-report on the questionnaire. Separate questions were asked about whether the participants had ever been diagnosed for HBV and HCV, respectively, and therefore differentiation between HBV and HCV carrier status was possible.

Logistic regression models were used to calculate the odds ratios (OR) of awareness of hepatitis viral infection status among hepatitis carriers and their associations with demographic and lifestyle risk factors. Statistically significant demographic variables in the univariate analysis were included in the multivariate model, and stepwise selection was done to choose variables for the final models. Sex and age groups were included in all final models because significant differences between groups in the distributions of demographic and lifestyle habits were observed. All statistical analyses were done using SAS software (version 9.1.3 Service Pack 3, 2002-2003, SAS Institute).

The study protocol was approved by the Institutional Review Board of the National Cancer Center.

Results

A total of 18,636 persons agreed to participate in the main study. Among these, 679 participants failed to provide information on self-reported HBV infection status or to be measured for the HBV surface antigen. For HCV analysis, 711 subjects were excluded due to missing information on either self-reported HCV infection status or laboratory results for HCV antibody. Among the eligible study population, 904 (5.0%) subjects were HBV carriers and 146 (0.8%) were HCV carriers. Four persons were co-infected with HBV and HCV. These four people contributed to analyses for both HBV and HCV. Among the study subjects who provided information on the year they were first diagnosed with hepatitis viral infection, 51% of HCV carriers were diagnosed within the past 5 years, whereas 53% of HBV carriers were diagnosed more than 15 years ago (data not shown).

Among HBV carriers, 671 (74.2%) were aware of their infection status (Table 1). Younger participants were more likely to be aware of their infection status, although the ORs were not statistically significant. High school graduates and college graduates were 2.0 and 2.4 times more likely to be aware of their infection status than their counterparts with middle school or lower educations, respectively. After adjustment for age and other covariates, ORs for awareness of infection status were 1.58 [95% confidence interval (95% CI), 1.00-2.48] for high school graduates and 1.85 (95% CI, 1.18-2.90) for college graduates. Even after adjusting for age and other covariates, currently married or divorced/widowed persons were more likely to be aware of their infection status than unmarried persons. Persons having a family history of liver cancer or liver disease among first-degree relatives were 1.7 times more likely to be aware of their infection status than persons with no family history of liver diseases. Participants who were aware of their HBV carrier status were more likely to be former smokers (adjusted OR, 1.69; 95% CI, 1.04-2.74) or former drinkers (adjusted OR, 2.02; 95% CI, 1.01-4.06). The distribution of current smokers was similar between aware and unaware groups, and more than 60% of HBV carriers consumed alcohol regularly, regardless of awareness of their status.

Among the 146 HCV carriers, only 51 (34.9%) people were aware of their infection status (Table 2). In contrast to HBV infection, no measured demographic characteristics were significantly related with awareness of HCV infection status among HCV carriers. However, those who were aware of their infection status were much more likely to be former drinkers (adjusted OR, 9.18; 95% CI, 1.8-47.2).

Discussion

To our knowledge, this is the first study to investigate factors associated with awareness of viral infection status among HBV and HCV carriers. Among the current study population, awareness of HBV carrier status was significantly associated with certain demographic characteristics including marital status, educational level, and family history of liver cancer or liver disease. However, none of the demographic characteristics were significantly associated with awareness of HCV infection status among HCV carriers.

In this population, only one third of HCV carriers were aware of their infection status, which was much lower than the proportion of HBV carriers who were aware of their status. Because anti-HCV antibody testing is not a part of regular health check-ups provided by the NHIC and the prevalence of HCV is far lower than that of HBV among Koreans, the low level of awareness was not a surprising result. In Korea, in contrast to HCV infection, which typically occurs during adulthood, HBV infection is mainly transmitted vertically from HBV carrier mothers to their children. Risk factors for HCV infection in Korea include blood transfusions before the anti-HCV screening of blood donors in 1992, a history of surgical operations, and acupuncture (8).

It has been estimated that 70% of all HCC cases in Korea are HBV related and that 15% to 20% are HCV related (9). Because only ~10% of HCC cases are non-B, non-C HCC, surveillance of hepatitis carriers is the most important tool for the secondary prevention of HCC in Korea. The National Cancer Screening Program of Korea covers five major cancers: stomach, liver, colorectum, breast, and uterine cervix. Unlike other cancer sites, for which the eligibility for screening is determined by age only, liver cancer screening is provided to persons who are HBV or HCV carriers or have liver cirrhosis. Because HBV or HCV infection is usually asymptomatic, hepatitis viral carriers cannot recognize their eligibility for liver cancer screening if they are not aware of their infection status. Our data show that two thirds of HCV carriers and one fourth of HBV carriers were not aware of their infection status; therefore, a program to identify population groups at high risk for HCC should be implemented, along with improved compliance with HCC screening among high-risk groups.

Heavy alcohol consumption has been suggested as an independent risk factor for HCC development that acts synergistically with hepatitis viral infection (10-12). Cigarette smoking also both acts independently and interacts with hepatitis viral infection for HCC risk (13-16). Therefore, controlling smoking and alcohol consumption habits is a prudent strategy for preventing the development of HCC, especially in hepatitis viral infection carriers. In this study population, HBV carriers who were aware of their infection status were more likely to be former smokers or drinkers compared with HBV carriers who were not aware of their infection status, which suggests a favorable behavioral change for this group. Those who were aware of their HCV infection status were also more likely to be former drinkers. Still, more than half of hepatitis carriers were current drinkers, regardless of their awareness of their carrier status. The prevalence of smoking among adult men has dramatically decreased from 75.1% in 1992 to 43.4% in 2007 as a result of governmental and nongovernmental support and public concerns for the adverse health effects of cigarette smoking (17). However, adult alcohol consumption rates have increased in both men and women over the last few decades. Age-adjusted proportions of regular alcohol drinkers among people 20 to 59 years old were 49.1% (77.3% for men and 23.0% for women) in 1989 and 83.9% (90.6% for men and 77.0% for

Table 1. Awareness of HBV infection status among 904 HBV carriers and association between awareness and demographic factors and risk behaviors, National Cancer Center, Korea, 2002-2008

	Unaware, *n* (%)	Aware, *n* (%)	Crude OR (95% CI)	Adjusted OR* (95% CI)
Overall	233 (25.8)			
Sex				
Male	134 (25.3)	395 (74.7)	1.00 (reference)	1.00 (reference)
Female	99 (26.4)	276 (73.6)	0.95 (0.70-1.28)	1.08 (0.78-1.50)
Age (y)				
30-39	34 (24.8)	103 (75.2)	1.00 (reference)	1.00 (reference)
40-49	104 (23.8)	333 (76.2)	1.06 (0.68-1.65)	0.91 (0.56-1.47)
50-59	61 (26.3)	171 (73.7)	0.93 (0.57-1.50)	0.85 (0.50-1.44)
60+	34 (34.7)	64 (65.3)	0.62 (0.35-1.10)	0.68 (0.36-1.26)
Education level				
Middle or less	39 (34.2)	75 (65.8)	1.00 (reference)	1.00 (reference)
High school	76 (24.8)	231 (75.2)	2.02 (1.33-3.06)	1.58 (1.00-2.48)†
College or more	98 (21.8)	351 (78.2)	2.37 (1.60-3.54)	1.85 (1.18-2.90)†
Household income‡				
<2,000	34 (31.2)	75 (68.8)	1.00 (reference)	1.00 (reference)
2,000-4,000	54 (22.6)	185 (77.4)	2.01 (1.32-3.04)	1.39 (0.88-2.21)
>4,000	104 (22.5)	358 (77.5)	2.02 (1.41-2.89)	1.24 (0.78-1.96)
Marital status				
Unmarried	10 (37.0)	17 (63.0)	1.00 (reference)	1.00 (reference)
Married	192 (23.8)	616 (76.2)	3.32 (1.94-5.67)	2.82 (1.56-5.11)†
Divorced/Widowed	11 (29.7)	26 (70.3)	2.45 (1.02-2.84)	2.59 (1.03-6.50)†
Family history of liver cancer or disease				
No	185 (28.7)	460 (71.3)	1.00 (reference)	1.00 (reference)
Yes	48 (18.5)	211 (81.5)	1.77 (1.24-2.53)	1.70 (1.18-2.45)†
Smoking status				
Never smoker	100 (49.5)	287 (45.9)	1.00 (reference)	1.00 (reference)
Ex-smoker	31 (15.4)	144 (23.0)	1.70 (1.06-2.73)	1.69 (1.04-2.74)†
Current smoker	71 (35.2)	194 (31.0)	1.05 (0.74-1.50)	0.89 (0.55-1.45)
Alcohol consumption				
Never drinker	58 (28.4)	186 (29.3)	1.00 (reference)	1.00 (reference)
Ex-drinker	11 (5.4)	57 (9.0)	1.79 (0.91-3.51)	2.02 (1.01-4.06)†
Current drinker	135 (66.2)	391 (61.7)	1.11 (0.78-1.58)	1.28 (0.84-1.95)

*Adjusted for sex, age group, education level, marital status, and family history of liver disease or cancer.
†$P < 0.05$.
‡Unit is thousand won per month.

Table 2. Awareness of HCV infection status among 146 HCV carriers and the associations between awareness and demographic factors and risk behaviors, National Cancer Center, Korea, 2002-2008

	Unaware, *n* (%)	Aware, *n* (%)	Crude OR (95% CI)	Adjusted OR* (95% CI)
Overall	95 (65.1)			
Sex				
Male	48 (61.5)	30 (38.5)	1.00 (reference)	1.00 (reference)
Female	47 (69.1)	21 (30.9)	0.72 (0.36-1.42)	0.72 (0.36-1.44)
Age (y)				
30-39	12 (70.6)	5 (29.4)	1.00 (reference)	1.00 (reference)
40-49	31 (68.9)	14 (31.1)	1.08 (0.32-3.67)	1.09 (0.32-3.70)
50-59	29 (61.7)	18 (38.3)	1.49 (0.45-4.93)	1.48 (0.45-4.92)
60+	23 (62.2)	14 (37.8)	1.46 (0.42-5.03)	1.46 (0.42-5.04)
Education level				
Middle or less	16 (61.5)	10 (38.5)	1.00 (reference)	1.00 (reference)
High school	31 (59.6)	21 (40.4)	1.60 (0.65-3.93)	1.87 (0.73-4.77)
College or more	38 (66.7)	19 (33.3)	1.18 (0.48-2.89)	1.39 (0.54-3.56)
Household income†				
<2,000	17 (63.0)	10 (37.0)	1.00 (reference)	1.00 (reference)
2,000-4,000	22 (61.1)	14 (38.9)	1.43 (0.59-3.49)	1.65 (0.64-4.26)
>4,000	37 (63.8)	21 (36.2)	1.28 (0.58-2.83)	1.52 (0.62-3.76)
Marital status				
Unmarried	3 (60.0)	2 (40.0)	1.00 (reference)	1.00 (reference)
Married	73 (62.4)	44 (37.6)	1.66 (0.50-5.53)	1.64 (0.48-5.60)
Divorced/widowed	11 (78.6)	3 (21.4)	0.75 (0.14-4.17)	0.73 (0.13-4.25)
Family history of liver cancer or disease				
No	83 (64.3)	46 (35.7)	1.00 (reference)	1.00 (reference)
Yes	12 (70.6)	5 (29.4)	0.75 (0.25-2.27)	0.78 (0.26-2.38)
Smoking status				
Never smoker	51 (60.7)	21 (46.7)	1.00 (reference)	1.00 (reference)
Ex-smoker	11 (13.1)	12 (26.7)	2.00 (0.68-5.88)	1.92 (0.63-5.81)
Current smoker	22 (26.2)	12 (35.3)	0.75 (0.32-1.80)	0.83 (0.28-2.40)
Alcohol consumption				
Never drinker	20 (23.8)	14 (29.8)	1.00 (reference)	1.00 (reference)
Ex-drinker	2 (2.4)	8 (17.0)	9.92 (1.97-50.0)	9.18 (1.79-47.2)‡
Current drinker	62 (73.8)	25 (53.2)	1.74 (0.76-3.96)	2.33 (0.87-6.3)

*Adjusted for sex and age groups.
†Unit is thousand won per month.
‡$P < 0.05$.

women) in 2005 (17). Alcohol drinking is regarded as an important part of social gatherings in Korean culture, and regulations and tax policies for alcoholic beverages are not as strict as those applied for cigarettes. Cancer prevention campaigns in Korea advertise the importance of limiting alcoholic beverage consumption.[10] The development of effective strategies for delivering messages on the health effects of alcoholic beverages should be targeted to not only to the general population but also toward groups at high risk for liver disease.

The study population included participants for a cancer screening program and may therefore not represent the general Korean population. However, the prevalence of hepatitis viral carriers in the study population was comparable to that expected in the general population. Given the design, it is likely that our study participants pay more attention to their health status, and we expect that awareness of viral hepatitis carrier status in the general population would be lower than the proportion reported here. The population characteristics hardly affect the internal validity of the current study, which compared the distribution of demographic and risk factors between groups that were aware or not aware of their infection status.

In conclusion, two thirds of HCV carriers and one fourth of HBV carriers were not aware of their infection status in this cancer screenee population. Awareness of hepatitis infection status may affect other risk behaviors, such as alcohol drinking and cigarette smoking. Identifying high-risk groups for HCC and providing appropriate secondary prevention and guidelines for health behaviors should be pursued to reduce the disease burden for HCC.

[10] http://cancer.go.kr

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

Acknowledgments

The costs of publication of this article were defrayed in part by the payment of page charges. This article must therefore be hereby marked *advertisement* in accordance with 18 U.S.C. Section 1734 solely to indicate this fact.

References

1. Yoon SJ, Lee H, Shin Y, Kim YI, Kim CY, Chang H. Estimation of the burden of major cancers in Korea. J Korean Med Sci 2002;17:604–10.
2. El-Serag HB, Rudolph KL. Hepatocellular carcinoma: epidemiology and molecular carcinogenesis. Gastroenterology 2007;132:2557–76.
3. Fattovich G, Giustina G, Schalm SW, et al. Occurrence of hepatocellular carcinoma and decompensation in western European patients with cirrhosis type B. The EUROHEP Study Group on Hepatitis B Virus and Cirrhosis. Hepatology 1995;21:77–82.
4. Hu KQ, Tong MJ. The long-term outcomes of patients with compensated hepatitis C virus-related cirrhosis and history of parenteral exposure in the United States. Hepatology 1999;29:1311–6.
5. Serfaty L, Aumaitre H, Chazouilleres O, et al. Determinants of outcome of compensated hepatitis C virus-related cirrhosis. Hepatology 1998;27:1435–40.
6. The Third National Health and Nutritional Examination. Seoul: Ministry of Health and Welfare; 2007.

7. Shin HR, Hwang SY, Nam CM. The prevalence of hepatitis C virus infection in Korea: pooled analysis. J Korean Med Sci 2005;20:985–8.
8. Shin HR. Epidemiology of hepatitis C virus in Korea. Intervirology 2006;49:18–22.
9. Cho HH, Kim YH, Jung JM, et al. Clinical characteristics of non-B, non-C hepatocellular carcinoma and detection of HBV, HCV and TTV viremia. Korean J Hepatol 2001;7:439–48.
10. Donato F, Tagger A, Gelatti U, et al. Alcohol and hepatocellular carcinoma: the effect of lifetime intake and hepatitis virus infections in men and women. Am J Epidemiol 2002;155:323–31.
11. Hassan MM, Hwang LY, Hatten CJ, et al. Risk factors for hepatocellular carcinoma: synergism of alcohol with viral hepatitis and diabetes mellitus. Hepatology 2002;36:1206–13.
12. Morgan TR, Mandayam S, Jamal MM. Alcohol and hepatocellular carcinoma. Gastroenterology 2004;127:S87–96.
13. Franceschi S, Montella M, Polesel J, et al. Hepatitis viruses, alcohol, and tobacco in the etiology of hepatocellular carcinoma in Italy. Cancer Epidemiol Biomarkers Prev 2006;15:683–9.
14. Hassan MM, Spitz MR, Thomas MB, et al. Effect of different types of smoking and synergism with hepatitis C virus on risk of hepatocellular carcinoma in American men and women: case-control study. Int J Cancer 2008;123:1883–91.
15. Mori M, Hara M, Wada I, et al. Prospective study of hepatitis B and C viral infections, cigarette smoking, alcohol consumption, and other factors associated with hepatocellular carcinoma risk in Japan. Am J Epidemiol 2000;151:131–9.
16. Wang LY, You SL, Lu SN, et al. Risk of hepatocellular carcinoma and habits of alcohol drinking, betel quid chewing and cigarette smoking: a cohort of 2416 HBsAg-seropositive and 9421 HBsAg-seronegative male residents in Taiwan. Cancer Causes Control 2003;14:241–50.
17. Cancer facts & figures 2008 in Korea. Goyang-si: National Cancer Center; 2008.