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Sex Differences Associated With Hepatitis B Virus Surface Antigen Seropositivity Unwareness in Hepatitis B Virus Surface Antigen-positive Adults: 2007-2012 Korea National Health and Nutrition Examination Survey

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Objectives: To examine the sex-specific factors associated with being unaware of one's hepatitis B virus surface antigen (HBsAg) seropositivity status in a large, HBsAg-positive population of Koreans.

Methods: In total, 1197 subjects aged 19 years or older who were HBsAg-positive according to data from the 2007-2012 Korea National Health and Nutrition Examination Survey were included. Subjects were considered unaware of their HBsAg seropositivity status if they answered that they had no knowledge of being previously infected by the hepatitis B virus (HBV) or diagnosed with HBV hepatitis. Multivariate Poisson regression models with robust variance estimate were used to assess the significance of the variables using weighted frequencies.

Results: The majority (77.8%) of HbsAg-positive Korean adults (females, 81.9%; males, 74.6%) were unaware of their HBsAg seropositivity status. We found that sex (female: prevalence ratio [PR] 1.19), household income (low: PR, 1.15), marital status (never married: PR, 1.18), self-rated health (moderate: PR, 1.14; good: PR, 1.12), and alcohol use (at least 2-3 times/wk: PR, 1.21) were associated with being unaware. In females, age (50 to 59 years: PR, 1.29; ≥70 years: PR, 1.30), household income (low: PR, 1.37; middle−low: PR, 1.24), and marital status (never married: PR, 1.33) were associated with being unaware. In males, self-rated health (moderate: PR, 1.14; good: PR, 1.21) and alcohol use (at least 2−3 times/wk: PR, 1.21) were associated with being unaware.

Conclusions: Factors related to the socioeconomic status of females and the health-related behaviors of males were found to be associated with being unaware of one's HBsAg seropositivity status.

Key words: Hepatitis B virus, Korea, Carcinoma, Hepatocellular, Awareness

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INTRODUCTION

Liver cancer is the second most common cause of death from cancer worldwide, estimated to be responsible for nearly 746 000 deaths in 2012 (9.1% of all cancer-related deaths) [1]. The prognosis for liver cancer is very poor, with a 5-year survival rate of 28.6% from 2007 to 2011 in the Republic of Korea (hereafter Korea). As a result, the geographical patterns of the incidence and mortality of liver cancer are similar [1]. In 2011, liver cancer

was the fourth most common cancer in Korean males (35.6 per 100 000, age-adjusted incidence using the world standard population) and the sixth most common cancer in Korean females (10.3 per 100 000) [2]. In addition, liver cancer was the second most common cause of cancer death in Korean males (24.3 per 100 000) and the fourth most common cancer death in Korean women (6.1 per 100 000) [2]. Hepatitis B virus (HBV) infection is known as a major risk factor for the development of hepatocellular carcinoma among patients with chronic HBV infections [3]. Since the national HBV vaccination program began in Korea in 1985, the prevalence of seropositivity has decreased, primarily due to the dramatic decrease in the prevalence among adolescents and younger adults [4].

The National Cancer Screening Program (NCSP) in Korea provides liver cancer screening services to Medical Aid Program recipients and National Health Insurance beneficiaries. Although the National Cancer Center recommends ultrasonography and serum alpha-fetoprotein screenings every six months for anyone at high risk for liver cancer, the NCSP provides ultrasonography and serum alpha-fetoprotein testing only for males and females 40 years of age or older with chronic HBV infection, hepatitis C virus (HCV) infection, or liver cirrhosis [5,6].

Previous studies have shown that infected individuals who are aware of their HBV surface antigen (HBsAg) seropositivity status are more likely to participate in a liver cancer screening program [7,8]. Although this awareness is the first step towards participation in a liver cancer screening program, relatively little is known about the factors associated with being unaware of one's HBsAg seropositivity status. A previous study suggested that females are less likely to participate in hepatocellular carcinoma screening than males [9]. Furthermore, females tend to be more socially disadvantaged than males are in Korea. Therefore, the purpose of this study was to examine sex-specific factors associated with being unaware of one's HBsAg seropositivity status in a representative population of Koreans using the Korea National Health and Nutrition Examination Survey (KNHANES).

METHODS

Subjects

Data from the KNHANES IV and V collected annually from 2007 to 2012 were used in this study. The KNHANES is a population-based cross-sectional survey that was conducted by the Korea Centers for Disease Control and Prevention. These sur-

veys used a stratified, multistage, clustered probability sampling method according to geographical area, age, and gender so that the results would be representative of the entire non-institutionalized Korean population in a given year. Trained interviewers conducted face-to-face interviews at participants' households using a structured questionnaire. The KNHANES is the only population-based survey that collects serum samples for testing HBsAg seropositivity status in Korea as well as information about the presence and awareness of each participant's HBsAg seropositivity status. All available serum samples were tested for HBsAg.

The total study population consisted of 63 301 individuals aged ≥1 year (6455 in 2007, 12 528 in 2008, 12 722 in 2009, 10 938 in 2010, 10 589 in 2011, and 10 069 in 2012), of whom 50 405 individuals (4594 in 2007, 9744 in 2008, 10 533 in 2009, 8958 in 2010, 8518 in 2011, and 8058 in 2012) completed the survey. The average response rate was 79.6% (71.2% in 2007, 77.8% in 2008, 82.8% in 2009, 81.9% in 2010, 80.4% in 2011, and 80.0% in 2012). Serum samples from 39 167 participants were tested for HBsAg. Individuals who were younger than 19 years of age (6541 males and 5859 females) or whose blood tests were negative for HBsAg (16 746 males and 21 256 females) were excluded. We further excluded 80 individuals with missing data. Therefore, of the 50 405 subjects who completed the KNHANES surveys during 2007-2012, we analyzed 1197 subjects who were 19 years of age or older and HBsAg-positive (Table 1).

Variables

Dependent variable

Being unaware of one's HBsAg seropositivity status was defined as having a positive HBsAg blood test, but responding in the face-to-face interview that they had never been infected by the HBV.

Independent variables

To our knowledge, no previous studies have investigated factors associated with being unaware of one's HBsAg seropositivity status. Therefore, we selected independent variables from those associated with liver cancer screening tests or the prevalence of HBsAg seropositivity, which included sex, income, age, smoking, alcohol intake, private insurance, residential area, and self-rated health [4,9,10] as well as other potential confounding factors. In this study, age, education level, residential area, marital status, occupation, receiving a health examination in the

Table 1. General characteristics of the study population

Characteristics	Total	Males	Females
Age (y)			
19-39	348 (34.5)	169 (35.5)	179 (33.4)
40-49	293 (28.6)	149 (30)	145 (26.9)
50-59	271 (22.8)	141 (24.2)	130 (21)
60-69	183 (9.2)	82 (7.1)	101 (11.9)
≥70	101 (4.9)	42 (3.2)	59 (7)
Household income quartiles			
Low	197 (12)	78 (9.6)	119 (15.1)
Middle-low	308 (26.1)	143 (23.4)	165 (29.5)
Middle-high	312 (28.9)	164 (30.4)	148 (26.9)
High	378 (33.1)	197 (36.6)	181 (28.6)
Educational level			
Elementary school	270 (16.9)	81 (10.2)	189 (25.3)
Middle school	148 (11)	74 (10.3)	74 (11.8)
High school	406 (38.5)	206 (39)	200 (37.8)
College or higher	371 (33.7)	221 (40.4)	150 (25.1)
Residential area			
Urban	912 (80.4)	439 (80.7)	473 (80)
Rural	283 (19.6)	143 (19.3)	140 (19.9)
Marital status			
Married/cohabitation	958 (77.5)	491 (79.3)	467 (75.3)
Divorced/separated/widowed	140 (9.7)	29 (4.2)	111 (16.8)
Never married	97 (12.7)	62 (16.5)	35 (3.5)
Occupation			
White collar	392 (35.6)	225 (41.4)	167 (28.2)
Blue collar	373 (32.1)	254 (43.1)	119 (18)
None or homemaker	430 (32.3)	103 (15.4)	327 (53.8)
Health examination			
Yes	717 (59.1)	366 (60.9)	351 (56.9)
No	478 (40.9)	216 (39.1)	262 (43.1)
Private health insurance			
Yes	870 (78.1)	422 (79.5)	448 (76.3)
No	325 (21.9)	160 (20.5)	165 (23.7)
Self-rated health			
Poor	286 (20.5)	115 (17)	171 (25)
Moderate	566 (52.3)	282 (55.4)	284 (48.4)
Good	343 (27.1)	185 (27.6)	158 (26.6)
Cigarette smoking			
Never	666 (48.9)	111 (18.5)	555 (87.6)
Former	113 (10.5)	100 (16.4)	3 (3.0)
Current	416 (40.5)	371 (65)	45 (9.4)
Alcohol use			
Never	363 (25.2)	121 (16.7)	242 (35.9)
1-4 times/mo	579 (50.5)	246 (45.6)	333 (56.7)
≥2-3 times/wk	253 (24.4)	215 (37.7)	38 (7.4)

(Continued to the next)

Table 1. Continued

Characteristics	Total	Males	Females
Body mass index (kg/m²)			
<18.5	35 (3.3)	14 (2.7)	21 (4.1)
18.5-23.9	597 (1.7)	267 (46.1)	330 (56.4)
24-26.9	388 (30.6)	215 (34.5)	173 (25.8)
≥27.0	175 (15.4)	86 (16.6)	89 (13.8)
Awareness of hepatitis B surface antigen positivity			
Unaware	933 (77.8)	438 (74.6)	495 (81.9)
Aware	262 (22.2)	144 (25.4)	118 (18.1)
Total	1197 (100)	583 (48.7)	614 (51.3)

Values are presented as number (weighted %).

previous two years, private health insurance status, self-rated health status, cigarette smoking, frequency of alcohol use, and body mass index (BMI) were compared between the sex-specific groups to determine factors related to being unaware of one's HBsAg seropositivity status.

Based on the age divisions in the NCSP's guidelines for liver cancer screening among those 40 years of age and older, subjects were divided into five age groups: 19 to 39 years, 40 to 49 years, 50 to 59 years, 60 to 69 years, and 70 years of age or older. Education level was categorized according to the highest level completed as elementary school, middle school, high school, or college and higher. Residential areas were categorized as urban or rural. Marital status was categorized as married and cohabitating with a partner, divorced/separated/widowed, or never married. Occupation was divided into three categories: white collar (administrative, engineering, science, teaching and related occupations, sales and related occupations, and service), blue collar (farming, forestry, fishing, hunting, carpentry, machine operators, fabricators, and laborers), and unemployed (including homemakers and students). In addition, participants were asked if they had received a general health examination, regardless of its type, in the last two years. Self-rated health status was categorized as good (good or very good), moderate, or poor (poor or very poor). BMI was divided into four categories: <18.5 kg/m², 18.5-23.9 kg/m², 24.0-26.9 kg/m², and ≥27.0 kg/m² [11-13].

Statistical analysis

For all analyses, sample weights were included and weighted frequencies were computed. We tested baseline associations between all variables with chi-square tests. Multivariate Poisson regression models with robust variance estimates were

used to assess the significance of the variables described above and to calculate prevalence ratios (PR) and 95% confidence intervals (CI) [14]. Moreover, trend tests were performed across age and household income categories. All of the aforementioned variables were included in the multivariate logistic regression analysis. All hypotheses were tested using two sided tests and a *p*-value less than 0.05 was deemed statistically significant. All statistical analyses were performed using SAS version 9.3 (SAS Institute Inc., Cary, NC, USA).

The institutional review board approval was waived because the KNHANES data are made publically available for scientific use.

RESULTS

The general characteristics of the study population are shown in Table 1. Of the 1197 individuals included in this study, 583 were males and 614 were females. There were 438 (74.6%) males and 495 (81.9%) females who were unaware of their HBsAg seropositivity status, and this difference was statistically significant between sex. In the total population, 77.8% of HbsAg-positive Korean adults were unaware of their HBsAg seropositivity status.

Table 2 shows the characteristics of the study population divided between those who were aware or unaware of their HBsAg seropositivity. Awareness significantly differed by sex (*p*=0.007) and the frequency of alcohol use (*p*=0.018). Among males, self-rated health status (*p*=0.038) and the frequency of alcohol use (*p*=0.006) significantly differed between the awareness groups. Among females, there were significant differences between the two groups for household income (*p*=0.002), education level (*p*=0.039), and marital status (*p*=0.003).

Table 3 shows the results of the multivariate Poisson regression models with robust variance estimates, with unawareness of one's HBsAg seropositivity as the outcome. After adjusting for all potential confounders, the prevalence of being unaware of one's HBsAg seropositivity was 1.19 times higher (95% CI, 1.06 to 1.43) in females than that in males was. The prevalence of being unaware of one's HBsAg seropositivity was 1.15 times higher (95% CI, 1.02 to 1.30) among those with a low income than that among those with a high income was. Those who were never married had a 1.18 times higher (95% CI, 1.03 to 1.36) prevalence than those who were married and cohabitating with their partner did. The prevalence of being unaware of one's HBsAg seropositivity for subjects with good and moderate self-rated

health was 1.14 times higher (95% CI, 1.03 to 1.26) and 1.12 times higher (95% CI, 1.01 to 1.12), respectively, than that for subjects with poor self-rated health was. Subjects who used alcohol at least 2-3 times/wk had a 1.21 times higher (95% CI, 1.09 to 1.35) prevalence than those who never used alcohol did.

In females, the prevalence of being unaware of one's HBsAg seropositivity among those aged 50 to 59 years and ≥70 years was 1.29 times higher (95% CI, 1.07 to 1.54) and 1.30 times higher (95% CI, 1.04 to 1.64), respectively, than that for those who were 19 to 39 years was. The prevalence of being unaware of one's HBsAg seropositivity among those with middle-low incomes or low incomes were 1.24 times higher (95% CI, 1.10 to 1.41) and 1.37 times higher (95% CI, 1.17 to 1.59), respectively, than that among those with high incomes was. Females who were never married had a 1.33 times higher (95% CI, 1.16 to 1.53) prevalence than females who were married and cohabitating with their partner did. Moreover, the prevalence of being unaware of one's HBsAg seropositivity in females who used alcohol at least 2-3 times/wk was 1.21 times higher (95% CI, 1.06 to 1.38) than that in females who never used alcohol was.

In males, the prevalence of being unaware of one's HBsAg seropositivity among those with good and moderate self-rated health was 1.23 times higher (95% CI, 1.01 to 1.50) and 1.29 times higher (95% CI, 1.07 to 1.55), respectively, than that among those with poor self-rated health was. In addition, men who used alcohol at least 2-3 times/wk had a 1.21 times higher (95% CI, 1.03 to 1.41) prevalence than those who never used alcohol did.

DISCUSSION

We found that a very large proportion (77.8%) of HBsAg-positive Korean adults was unaware of their HBsAg seropositivity status. Our result is similar to that of a study in the US in which approximately 65% and 75% of the infected population were unaware that they were infected with HBV and HCV, respectively [15]. However, a study from Canada reported that 54.5% of their respondents had tested positive for a current HBV infection and 69.5% of those with a sero-confirmed HCV infection reported having been diagnosed with those infections [16]. In a European study, an average of 78.5% were not aware that they had viral hepatitis at the time of their infection (77% for HBV and 80% for HCV), and 73% did not know that they were at risk for both HBV and HCV [17]. In Italy, the proportion of those unaware of their infection was 40.3% among patients who were admitted at one Italian hospital [18,19]. In a Polish

Table 2. The awareness of one's hepatitis B surface antigen (HBsAg) seropositivity status among HBsAg-positive Korean adults across various socio-demographic characteristics

Variables	Total		p-value	Males		p-value	Females		p-value
	Unaware	Aware		Unaware	Aware		Unaware	Aware	
Sex			0.007						
Male	438 (74.6)	144 (25.4)							
Female	495 (81.9)	118 (18.1)							
Age (y)			0.39			0.25			0.10
19-39	267 (76.1)	80 (23.9)		127 (74.1)	41 (25.9)		140 (78.7)	39 (21.3)	
40-49	223 (76.7)	70 (23.3)		110 (73.9)	39 (26.1)		113 (80.8)	31 (19.2)	
50-59	203 (77.9)	68 (22.1)		96 (71.8)	45 (28.2)		107 (86.8)	23 (13.2)	
60-69	153 (82.1)	30 (17.3)		73 (89.3)	9 (10.7)		80 (77.6)	21 (22.4)	
≥70	87 (86.1)	14 (13.9)		32 (72.5)	10 (27.5)		55 (94)	4 (6)	
Household income			0.02			0.71			0.002
Low	174 (86.2)	23 (13.8)		66 (79.7)	12 (20.3)		108 (91.5)	11 (8.5)	
Middle-low	254 (82.4)	54 (17.6)		112 (76.9)	31 (23.1)		142 (87.9)	23 (12.1)	
Middle-high	227 (74.6)	85 (25.4)		115 (71.6)	49 (28.4)		112 (78.9)	36 (21.1)	
High	278 (73.9)	100 (26.1)		145 (74.1)	52 (25.9)		133 (73.4)	48 (26.6)	
Education level			0.14			0.26			0.04
Elementary school	225 (84.5)	45 (15.5)		64 (79.6)	17 (20.4)		161 (87)	28 (13)	
Middle school	111 (78.2)	37 (21.8)		59 (80.6)	15 (19.4)		52 (75.5)	22 (24.5)	
High school	313 (76.7)	93 (23.3)		159 (76.3)	47 (23.7)		154 (77.4)	46 (22.6)	
College or higher	284 (75.5)	87 (24.5)		156 (70.1)	65 (29.9)		128 (86.6)	22 (13.4)	
Residential area			0.24			0.21			0.66
Urban	702 (76.9)	210 (23.1)		323 (73.3)	116 (26.7)		379 (81.5)	94 (18.5)	
Rural	231 (81.5)	52 (18.5)		115 (79.9)	28 (20.1)		116 (83.5)	24 (16.5)	
Marital status			0.14			0.93			0.003
Married/cohabitation	733 (76.2)	225 (23.8)		371 (74.2)	120 (25.8)		362 (78.9)	105 (21.1)	
Divorced/separated/widowed	122 (84.2)	18 (15.3)		22 (73.9)	7 (26.1)		100 (88.2)	11 (11.8)	
Never married	78 (82.1)	19 (17.9)		45 (76.4)	17 (23.6)		33 (97.2)	2 (2.8)	
Occupation			0.21			0.21			0.77
White collar	294 (74.4)	98 (25.6)		159 (70.3)	66 (29.7)		135 (82.1)	32 (17.9)	
Blue collar	299 (79.7)	74 (20.7)		201 (78.2)	53 (21.8)		98 (84.4)	21 (15.6)	
None or homemaker	340 (79.6)	90 (20.4)		78 (75.9)	25 (24.1)		262 (81)	65 (19)	
Health examination			0.52			0.88			0.45
Yes	547 (77)	170 (23)		273 (74.3)	93 (25.7)		274 (80.7)	77 (19.3)	
No	386 (78.9)	92 (21.1)		165 (74.9)	51 (25.1)		221 (83.5)	41 (16.5)	
Private health insurance			0.33			0.54			0.57
Yes	667 (77.1)	203 (22.9)		314 (74)	108 (26)		353 (81.3)	95 (18.7)	
No	266 (80.2)	59 (19.8)		124 (76.9)	36 (23.1)		142 (83.8)	23 (16.2)	
Self-rated health			0.13			0.04			0.76
Poor	208 (72.1)	78 (27.9)		73 (63.2)	42 (36.8)		135 (79.8)	36 (20.2)	
Moderate	448 (79.7)	118 (20.3)		220 (78.1)	62 (21.9)		228 (82.1)	56 (17.9)	
Good	277 (78.4)	66 (21.6)		145 (74.5)	40 (25.5)		132 (83.5)	26 (16.5)	
Cigarette smoking			0.30			0.82			0.18
Never	531 (80)	135 (20)		81 (72.4)	30 (27.6)		450 (82.1)	105 (17.9)	
Former	83 (74.8)	30 (25.2)		76 (76.8)	24 (23.2)		7 (60.7)	6 (39.3)	
Current	319 (75.9)	97 (24.1)		281 (74.6)	90 (25.4)		38 (86.8)	7 (13.2)	

(Continued to the next page)

Table 2. Continued from the previous page

Variables	Total		p-value	Males		p-value	Females		p-value
	Unaware	Aware		Unaware	Aware		Unaware	Aware	
Alcohol use			0.02			0.006			0.14
Never	283 (77)	80 (23)		89 (68.9)	32 (31.1)		194 (81.8)	48 (18.2)	
1-4 times/mo	441 (74.9)	138 (25.1)		174 (69.4)	72 (30.6)		267 (80.5)	66 (19.5)	
≥2-3 times/wk	209 (84.6)	44 (15.4)		175 (83.3)	40 (16.7)		34 (93.1)	4 (6.9)	
Body mass index (kg/m^2)			0.81			0.84			0.52
<18.5	28 (84.8)	7 (15.2)		12 (83.2)	2 (16.8)		16 (86.2)	5 (13.8)	
18.5-23.9	467 (77.1)	130 (22.9)		203 (73.9)	64 (26.1)		264 (80.4)	66 (19.6)	
24-26.9	302 (78)	86 (22)		156 (73.5)	59 (26.5)		146 (85.7)	27 (14.3)	
≥27.0	136 (78.2)	39 (21.8)		67 (77.3)	19 (22.7)		69 (79.6)	20 (20.4)	
Total	933 (77.8)	262 (22.2)		438 (74.6)	144 (25.4)		495 (81.9)	118 (18.1)	

Values are presented as number (weighted %).

Table 3. Factors associated with being unaware of one's hepatitis B surface antigen seropositivity status using multivariate Poisson regression models with robust variance estimates

	Total		Males		Females	
	PR	95% CI	PR	95% CI	PR	95% CI
Sex						
Male	1.00					
Female	1.19**	1.06, 1.43				
Age (y)						
19-39	1.00		1.00		1.00	
40-49	1.04	0.93, 1.16	0.96	0.81, 1.13	1.15	0.99, 1.32
50-59	1.06	0.93, 1.21	0.91	0.75, 1.10	1.29**	1.07, 1.54
60-69	1.11	0.96, 1.30	1.14	0.94, 1.38	1.1	0.87, 1.39
≥70	1.14	0.96, 1.36	0.94	0.70, 1.25	1.30*	1.04, 1.64
p for trend	0.15		0.98		0.047	
Household income						
High	1.00		1.00		1.00	
Mid-high	1.00	0.90, 1.11	0.92	0.79, 1.07	1.12	0.99, 1.28
Mid-low	1.09	0.98, 1.21	0.97	0.83, 1.13	1.24***	1.10, 1.41
Low	1.15*	1.02, 1.30	1.02	0.84, 1.24	1.37***	1.17, 1.59
p for trend	0.02		1.00		<0.001	
Education						
Elementary school	1.00		1.00		1.00	
Middle school	0.98	0.87, 1.10	1.01	0.84, 1.20	0.9	0.75, 1.07
High school	0.99	0.88, 1.21	0.96	0.81, 1.14	1.00	0.85, 1.18
College or higher	1.05	0.91, 1.20	0.94	0.76, 1.18	1.19	1.00, 1.43
Residential area						
Urban	1.00		1.00		1.00	
Rural	1.02	0.94, 1.11	1.05	0.92, 1.20	0.95	0.85, 1.06
Marital status						
Married/cohabitation	1.00		1.00		1.00	
Divorced/separated/widowed	1.04	0.93, 1.17	0.99	0.76, 1.30	1.03	0.91, 1.17
Never married	1.18*	1.03, 1.36	1.07	0.87, 1.33	1.33***	1.16, 1.53

Table 3. Continued from the previous page

	Total		Males		Females	
	PR	95% CI	PR	95% CI	PR	95% CI
Occupation						
White collar	1.00		1.00		1.00	
Blue collar	1.08	0.97, 1.20	1.09	0.93, 1.27	1.05	0.91, 1.20
None or homemaker	1.01	0.92, 1.11	1.08	0.89, 1.31	0.99	0.89, 1.09
Health examination						
Yes	1.00		1.00		1.00	
No	1.01	0.94, 1.09	0.98	0.86, 1.11	1.06	0.98, 1.15
Private health insurance						
Yes	1.00		1.00		1.00	
No	0.98	0.89, 1.09	1.05	0.91, 1.21	0.94	0.83, 1.07
Self-rated health						
Poor	1.00		1.00		1.00	
Moderate	1.14*	1.03, 1.26	1.29**	1.07, 1.55	1.04	0.93, 1.17
Good	1.12*	1.01, 1.26	1.23*	1.01, 1.50	1.07	0.95, 1.21
Cigarette smoking						
Never	1.00		1.00		1.00	
Former	0.99	0.86, 1.13	1.02	0.88, 1.17	0.71	0.42, 1.20
Current	1.01	0.90, 1.12	0.99	0.85, 1.16	0.98	0.84, 1.13
Alcohol use						
Never	1.00		1.00		1.00	
1-4 times/mo	1.00	0.92, 1.10	1.01	0.85, 1.20	1.00	0.91, 1.09
≥2-3 times/wk	1.21***	1.09, 1.35	1.21*	1.03, 1.41	1.21***	1.06, 1.38
Body mass index (kg/m^2)						
<18.5	1.1	0.94, 1.29	1.17	0.86, 1.58	0.99	0.82, 1.19
18.5-23.9	1.00		1.00		1.00	
24-26.9	1.02	0.94, 1.11	1.00	0.88, 1.13	1.06	0.97, 1.17
≥27.0	1.03	0.93, 1.14	1.06	0.91, 1.24	0.97	0.85, 1.11

PR, multivariate-adjusted prevalence ratio; CI, confidence interval.
*$p<0.05$, **$p<0.01$, ***$p<0.001$.

study, approximately 83.7% of all infected individuals were unaware of their HBV infection [20]. Despite the importance of HBV infections in public health, these data suggest that only a small proportion of HBV-infected individuals worldwide are aware of their seropositivity status. Due to this low level of awareness about HBV infections, it has been recommended that national programs aimed at increasing the awareness about the status of HBV infections be created [21].

In one study that used data from KNHANES-IV, the proportion of individuals who were unaware of their HBsAg seropositivity was 76.3% [7]. However, in a cancer screening study conducted at the Center for Cancer Early Detection and Prevention at the National Cancer Center in Korea, the proportion of those unaware was 21.6% [8]. In the latter study, the subjects were already participating in a cancer screening examination; therefore, the study population was not representative of the general population and was more likely to be aware of their HBsAg seropositivity than perhaps the general population is.

In the present population-based, cross-sectional study of Korean adults, the factors associated with being unaware of one's HBsAg seropositivity status were self-rated health and alcohol use in males and age, household income, marital status, and alcohol use in females. One novel finding of these results is the differences in associated factors between males and females. Whereas socioeconomic factors (household income and marital status) and age were the primary factors in females, only health-related variables (self-rated health status and frequency of alcohol use) were primary factors in males.

In one study that used data from the 2007-2011 KNHANES, socioeconomic status was associated with participation in opportunistic liver cancer screening, but not associated with organized screening in both sexes [10]. In the present study, being aware of one's HBsAg seropositivity status, which is the first step towards participation in a liver cancer screening program, was only associated with socioeconomic status among females. However, the frequency of alcohol use was an associated factor in both sexes. Two studies have reported that alcohol is associated with the presence of severe liver disease and the development of hepatocellular carcinoma in patients with an HBV infection [22,23]. Individuals who had been aware of their HBsAg seropositivity are expected to be more likely to quit using alcohol, therefore the association between alcohol use and unawareness might be reverse causation.

One possible explanation for the high PR in the present study among women who never married is that because a women's HBV infection status is a major concern during childbirth and these women are assumed to have no children, these women would be more likely to be unaware of their HBsAg seropositivity. Although the serum HBsAg test is widely included in the general health examination programs throughout Korea, self-reported participation in these general health examination programs was not associated with awareness in either sex.

According to the 2012 Korea Health Statistics report, the proportion of those who were unaware of having diabetes and hypertension decreased with increasing age and was higher in males than in females [24]. In contrast, in the present study, the prevalence of females who were unaware of their HBsAg seropositivity tended to increase with increasing age (*p* for trend <0.034), but no significant association with age was found in males. In addition, females had a 1.19 times higher prevalence of being unaware of their HBsAg seropositivity than that among males was. This relatively higher awareness among males might be because males have more opportunities than females do to learn of their HBsAg seropositivity status through employment and/or military service. The factors associated with being aware of one's HBsAg seropositivity seem to be different from those associated with being aware of having diabetes and hypertension; therefore, these findings suggest that different approaches to increase the awareness of one's disease status are needed.

Importantly, females with a low income (*p* for trend <0.001) and who were older (*p* for trend=0.047) were significantly more likely to be unaware of their HBsAg seropositivity status. The incidence of hepatocellular carcinoma is higher in individuals aged between 60 to 79 years old in Korea [25,26]. Our results suggest that a considerable proportion of these older individuals who are also socioeconomically disadvantaged may be at a high risk for developing hepatocellular carcinoma and be at a high risk for not being aware of their infection status. These factors may lead to a reduced likelihood of early cancer detection in these individuals. Awareness of one's HBsAg seropositivity status was found to be associated with an increased likelihood of being tested by a liver cancer screening program [7,8]. For breast cancer screening, females who perceived their risk of breast cancer to be high or had a history of benign breast disease were more likely to participate in breast cancer screening programs than their counterparts were [27]. This finding suggests that strategies focused on increasing the awareness among women of their HBsAg seropositivity status might have a substantial impact on their future participation in liver cancer screening programs.

Our study has several limitations. First, this study was cross-sectional; therefore, only associations, not causality, can be demonstrated. However, it can be speculated that age, household income, and marital status might be causal factors related to the awareness of one's HBsAg seropositivity status. Second, all data used in the present study, with the exception of the HBsAg status, were based on self-reports that are subject to information bias. However, except for the data collected on whether subjects had received a recent general health examination, the other independent variables in this study are relatively less subject to recall bias. Third, the dependent variable, being unaware of one's HBsAg seropositivity status, was defined based on responses to the question, "Have you ever been infected with HBV hepatitis?" However, a more accurate definition of one's HBsAg seropositivity status would have been ascertained by directly asking subjects about their HBsAg seropositivity status or knowledge of being a HBV carrier, but these data are not available in the KNHANES. In addition, a few individuals might have been incorrectly designated to the unawareness group because they differentiated between their HBsAg seropositivity status and having HBV hepatitis. Fourth, having a high education level has been found to be positively associated with participation in opportunistic liver cancer screenings, but not in organized screening [10]. We found the prevalence of being unaware of one's HBsAg status to be slightly higher among females with at least a college degree than that among females with a lower education level was. This result might be due to the incorrect designation of females who were highly knowledgeable about

their health and medicine. Nevertheless, the number of highly knowledgeable individuals is still likely to be substantially small when compared to the entire study population. Further studies are needed to investigate whether there is a high prevalence of females who are unaware of their HBsAg status among highly educated females. Fifth, no data were available on whether participants of the KNHANES had ever had their HBsAg tested previously. This data might have been a useful addition as a covariate. Therefore, it is possible that the factors we found to be related to awareness are actually related to a previous experience of undergoing an HBsAg test. Because these data were not available, we included data on whether subjects had received a general health examination in the previous two years, but this variable was not associated with awareness. Nevertheless, this variable only requested information on the previous two years and it is unknown whether an HBsAg test was included in the general health examination. Yet, we expect that the prevalence of HBsAg testing is quite high since Korean adults have access to this test through employment, military service, childbirth, and general health examinations given the known importance and high prevalence of hepatitis B in Korea.

Despite these limitations, representative data were used in this study; therefore, our findings are generalizable to the broader general population of Korea. Moreover, this study is the first large, population-based study, to our knowledge, investigating factors associated with being unaware of one's HBsAg seropositivity status. Several studies have reported on the proportion of those who are unaware of their HBsAg seropositivity status, but associated factors were not investigated [7,8,20].

In conclusion, we found that factors related to socioeconomic status in females and several health-related factors in males are associated with being unaware of one's HBV infection status in the Korean population, which suggests that social inequity might be more adversely affecting females than males. Considering that awareness is the first step toward participation in liver cancer screening programs, especially in females, improving this inequity might increase the chance of detecting liver cancer in its early stages. Thus, strategies to increase awareness and promote participation in liver cancer screening might positively affect females, especially those at a lower socioeconomic status.

The Korean economy has grown rapidly since the 1960s and the seroprevalence of HBsAg has been decreasing since the implementation of the national HBV vaccination program that began in 1985. Consequently, the burden and importance of hepatitis B has also been decreasing. However, the older Korean

generation, with a high seroprevalence of HbsAg, remains at a high risk for liver cancer with increasing age. Therefore, the burden of liver cancer in Korea is still considerably high despite the efforts of the vaccination program, and strategies to increase the public's awareness of their HBV infection status should be implemented, particularly those targeted at females with a low socioeconomic status.

CONFLICT OF INTEREST

The authors have no conflicts of interest with the material presented in this paper.

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