

Epidemiological Findings of Hepatitis B Infection Based on 1998 National Health and Nutrition Survey in Korea

The purpose of this study was to investigate the epidemiological characteristics of hepatitis B virus (HBV) infection in Korea based on the 1998 National Health and Nutrition Survey. Study subjects consisted of 9,771 aged 10 yr or over, who were selected from across Korea using a stratified multistage probability sampling design. The prevalence of hepatitis B surface antigen (HBsAg) was compared by age, sex, residency, household income, education, family history, family size, and frequency of eating out. The prevalence of HBsAg was 5.1% (95% confidence interval (CI): 4.5-5.7) in males and 4.1% (95% CI: 3.6-4.6) in females with a low prevalence in those under 20 yr old. Generally, HBsAg seropositivity by administrative area was similar with the exception of Jeju province. HBsAg seropositivity of Jeju island was approximately three times higher in both men and women, as compared with the national average. HBsAg seropositivity by socioeconomic status unexpectedly showed a very consistent positive association in both gender. Comparing HBsAg seropositivity by the frequency of eating out, in both gender, the more frequent they ate out, the higher it was. Our study suggested that there might be another transmission route of HBV, which is possibly related to diet.

Key Words : Hepatitis B; Korea; Geographical Variation; Socioeconomic Factors

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INTRODUCTION

Korea has been known to be one of the endemic areas in the world for hepatitis B virus (HBV) infection. According to one review article (1), the seropositivity of Hepatitis B surface antigen (HBsAg) was estimated to be 7 to 9% in the 1980s and about 60 to 70% of adults showed evidence of present or past HBV infection, although the figures varied somewhat depending on the characteristics of the study subjects and/or the HBV detection methods employed.

Although there have been many studies on the epidemiology of HBV infection in Korea, most of them were based on non-representative or small sized samples from selected communities. Fortunately, the Ministry of Health and Welfare (MOHW) of Korea performed a National Health and Nutrition Survey (NHNS) in 1998, which included selective serological markers for HBV infection (2). As the survey was based on a representative sample of the entire nation, this data can provide us a more comprehensive picture of the distribution of HBV infection in Korea.

The purpose of this study was to investigate the epidemiological characteristics of HBV infection in Korea based on the NHNS of 1998. More specifically, we wanted to see whether there was a geographical variation to seropositivity of HBsAg. If so, it might suggest a new clue to the transmission route of hepatitis B.

MATERIALS AND METHODS

Our study was based on the NHNS of 1998. The study design has been described in detail elsewhere (2). Briefly, the survey consisted of four parts; the Health Interview Survey, the Health Examination Survey, the Health Behavior Survey, and the Nutrition Survey. At first, 13,523 households were selected from across the nation using a stratified multistage probability sampling design and all the family members of those households were invited to participate in the study. A total of 12,283 households (participation rate: 90.8%) participated in the survey and 94 households of them were not family-connected, so the final sample consisted of 39,060 persons from 12,189 households.

With the exception of the Health Interview Survey, the other three surveys were carried out on a sub-sample, which was also randomly selected from the original sample. The final sub-sample consisted of 9,771 household members aged 10 yr or over from 4,828 households. Since the information necessary for this study was dispersed into all surveys, this study was based on the sub-sample.

For sex- and age-specific HBsAg seropositivity, all subjects of the final sub-sample were used. Comparing HBsAg seropositivity by demographic factors, 7,962 of the subjects aged 20 or over were included in the analyses, as the subjects aged less than 20 yr were mostly born after the introduction of

the vaccination program.

A 15 mL blood sample was collected from the study subjects and centrifuged within 30 min after sampling. The refrigerated sera were tested for HBsAg and hepatitis B surface antibody (anti-HBs) using ELISA tests (CODA of BIO-RAD company, California, U.S.A.) at a single laboratory. All procedures related with laboratory tests were thoroughly supervised by the quality control committee. Demographic and health behavior items were selected from the questionnaire, which was administered by trained interviewers.

We compared HBsAg seropositivity by age, sex, residency by administrative district (metropolitan city; city; rural), household income, education, family history of liver disease, family size, and frequency of eating out. All these variables were selected as possible risk factors, based on the results of other previous studies. If required, χ^2 test, test for trend, and logistic regression were performed by PC-SAS program.

RESULTS

Persons aged 10 yr or over showed HBsAg seropositivity of 5.1% in males and 4.1% in females. Among children and adolescents aged less than 20 yr, the positive rate was 2.1% in males and 2.7% in females. The age-specific rates showed the peak ages of positive rate as the twenties in

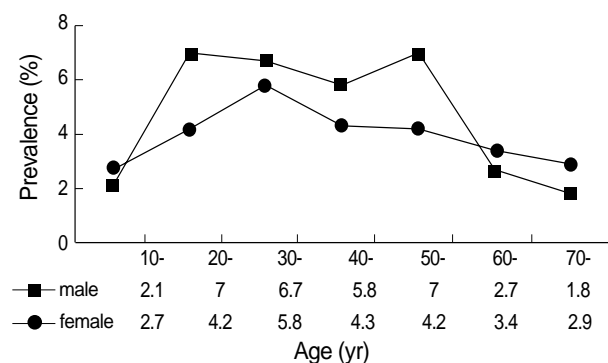


Fig. 1. Age-specific prevalence of HBsAg seropositivity based on 9,771 subjects aged 10 yr or over in Korea, 1998.

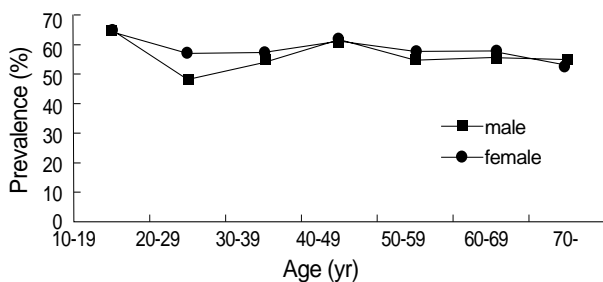


Fig. 2. Age-specific prevalence of anti-HBs seropositivity based on 9,771 subjects aged 10 yr or over in Korea, 1998.

males and thirties in females (Fig. 1). After that age, the rates showed plateaus of a sort until the fifties and then decreasing trends in both males and females. Seropositivity of anti-HBs of males and females were 57.0% and 58.9%, respectively. Age-specific anti-HBs positivity was the highest in those aged under 20 both in males and females (Fig. 2).

We compared the HBsAg seropositivity by administrative area (six metropolitan cities and nine provinces) among subjects aged 20 yr or more (Fig. 3). Those figures seemed to be rather similar, with the exception of Jeju province. On Jeju Island, located far from the main land, the HBsAg seropositivity was approximately three times higher in both males and females, as compared with the national average.

Seropositivity of HBsAg was compared by residency, household income, and education, which were selected as indices of socioeconomic status (Table 1). There was little difference seen among residency. However, the HBsAg seropositivity by household income showed clear positive relationships in both males and females ($p=0.001$ and $p=0.002$, respectively). After being stratified by residency, the relationship remained in all strata (Fig. 4). Moreover, after being stratified

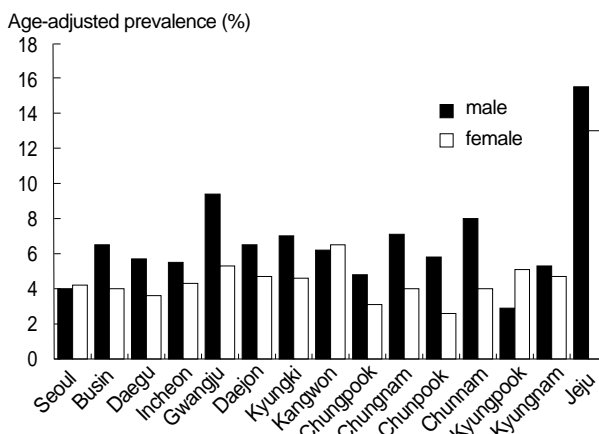


Fig. 3. Prevalence of HBsAg seropositivity by administrative area based on 7,962 subjects aged 20 yr or over in Korea, 1998.

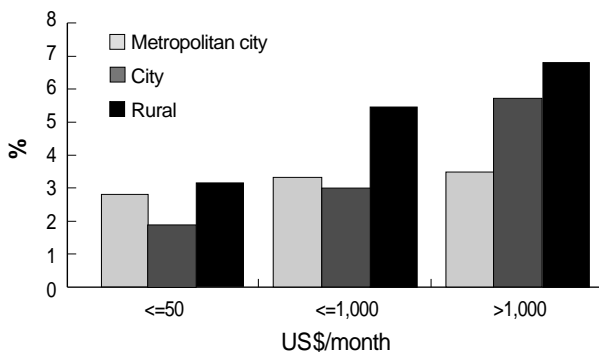


Fig. 4. Prevalence of HBsAg seropositivity according to household income and residency based on 7,962 subjects aged 20 yr or over in Korea, 1998.

Table 1. Seropositivity of HBsAg by socioeconomic status, family history of liver disease, family size, and frequency of eating out in Korea, 1998*

Variables	Categories	Male			Female		
		No.	%	<i>p</i> value [†]	No.	%	<i>p</i> value [†]
Residency	Metropolitan	1,430	5.5	0.694	1,719	4.3	0.904
	City	905	6.2		1,073	4.6	
	Rural	1,262	5.9		1,573	4.4	
Household income (US\$/month)	<500	693	3.5	0.001	978	2.9	0.002
	501-1000	1,048	5.3		1,249	4.1	
	1000-	1,856	7.0		2,138	5.3	
Education (yr)	<6	770	4.0	0.009	1,659	3.4	0.088
	7-9	508	5.3		621	6.1	
	10-	2,319	6.5		2,085	4.7	
Family history	No	3,421	5.1	0.001	4,091	4.1	0.001
	Yes	176	20.5		274	8.8	
Family size (number)	1-2	778	4.4	0.266	1,093	3.8	0.962
	3-4	2,029	6.4		2,280	5.0	
	5-	790	5.7		992	3.7	
Frequency of eating out	Rarely	1,281	4.2	0.003	2,133	3.9	0.003
	≥1/month	717	6.6		1,048	3.4	
	≥1/week	1,416	6.5		1,097	5.9	
	≥1/day	183	8.7		87	9.2	
Overall HBsAg seropositivity	Age ≥20 yr*	3,597	5.8	(5.0-6.6) [§]	4,365	4.4	(3.8-5.0) [§]
	Age ≥10 yr [†]	4,514	5.1	(4.5-5.8) [§]	5,257	4.1	(3.6-4.7) [§]

*: Based on 7,962 subjects aged 20 yr or over, [†]: *p* values are based on χ^2 test or test for trend, [‡]: Based on 9,771 subjects aged 10 yr or over, [§]: 95% confidence interval.

Table 2. Multiple logistic regression of the relationship between socioeconomic status, family history of liver disease, family size, and frequency of eating out risk factors and presence of HBsAg in Korea 1998*

Variables [†]	Categories	No.	Crude		Adjusted	
			OR	95% CI	OR	95% CI
Age (yr)	≥60	1,611	1.0		1.0	
	20-59	6,351	2.0	1.5, 2.8	1.5	1.0, 2.1
Sex	Female	4,365	1.0		1.0	
	Male	3,597	1.3	1.1, 1.6	1.3	1.0, 1.6
Province	Others	7,882	1.0		1.0	
	Jeju	80	3.4	1.8, 6.3	3.1	1.7, 5.9
Household income (US\$/month)	<500	1,671	1.0		1.0	
	501-1,000	2,297	1.5	1.1, 2.1	1.3	0.9, 1.8
	1,000-	3,994	2.0	1.5, 2.7	1.6	1.1, 2.6
Education (yr)	<6	2,429	1.0		1.0	
	7-	5,533	1.6	1.3, 2.0	1.0	0.7, 2.6
Family history	No	7,512	1.0		1.0	
	Yes	450	3.2	2.4, 4.3	3.2	2.4, 4.3
Family size	1-2	1,871	1.0		1.0	
	3-4	4,309	1.4	1.1, 1.9	1.0	0.8, 1.4
	5-	1,782	1.2	0.8, 1.6	0.8	0.6, 1.2
Frequency of eating out	<1/week	5,179	1.0		1.0	
	≥1/week	2,783	1.6	1.3, 1.9	1.3	1.1, 1.7

*: Based on 7,962 subjects aged 20 yr or over, [†]All variables included in the final model were displayed.

by administrative area, three out of six metropolitan cities and eight out of nine provinces showed positive associations between household income and HBsAg seropositivity (data was not shown). Regarding education level, a clear positive association was also seen in males ($p=0.009$).

Among those with a family history of liver disease, the risk of being HBsAg-positive was about four times higher in males (20.5% vs 5.1%; $p=0.001$) and twice higher in females (8.8% vs 4.1%; $p=0.001$) than those without a family history (Table 1). However, among HBsAg carriers, only 17.2% of males

and 12.5% of females demonstrated a family history of liver disease. The HBsAg seropositivity did not show any trend relating to the family size (Table 1). Comparing the HBsAg-positivity by the frequency of eating out in both males and females, the more frequent the subject ate out, the higher their HBsAg-positivity was ($p=0.003$ and $p=0.003$, respectively) (Table 1).

The simultaneously adjusted odds ratios are shown in Table 2. Age, sex, household income, province, family history of hepatitis, and frequency of eating out were all significantly associated with HBsAg seropositivity.

DISCUSSION

The present study is the first report for the status of HBV infection based on a representative sample from the whole population in Korea, even though there is no information concerning HBV vaccination history and several important risk factors related with HBV infection.

Seropositivity of HBsAg at 5.1% in males and 4.1% in females were approximately one-half or two-thirds of the figures seen in the 1980s (1), though there was no earlier study comparable to the present one in respect to study design. In particular, seropositivity of HBsAg among children and adolescents aged less than 20 was dramatically decreased to 2%, about one-third of those of earlier studies. All these findings reflect the effectiveness of Korea's vaccination program.

Except for those under 20 yr, the age-specific curves of HBsAg and/or anti-HBs positivity were very similar with those of studies performed before the introduction of the vaccination program. Generally, early studies showed their peak of seropositivity in twenties, a rather plateau until sixties, and then a decrease.

This study presents us at least two interesting findings, which could provide a clue to the transmission route of HBV. One is the higher HBsAg seropositivity among those living in Jeju Island and/or among those who eat out frequently. The other is an unexpectedly clear positive association between HBsAg seropositivity and socioeconomic status.

In this study, we compared HBsAg seropositivity among the various administrative areas. The HBsAg-positivity seemed to be similar across the areas with the exception of Jeju province. It is an interesting finding considering that Korea is a small country with a very homogenous population. Jeju province, an island located far from the main land, showed an approximately three times higher positivity than the national average, both in males and females. We examined the association of the variables analyzed with HBsAg seropositivity among persons living on Jeju Island. Although multivariate analysis was impossible due to the small sample size, the result was similar with that of the whole sample. This suggests that Jeju island is not different from other areas in Korea in terms of risk factors of HBV infection.

This is not the first study reporting a high HBsAg seropositivity in Jeju Island. Studies (3, 4) performed before the introduction of the hepatitis vaccination program also showed the same finding. So, it may be a true figure reflecting some environmental factors existing in Jeju Island, in relation to the high HBsAg seropositivity.

In addition, several papers from Korea reported a somewhat higher seropositivity in coast areas (5), small islands (6), or provinces with long coastlines (7), however, they were generally based on not-representative or small-sized samples. Other countries (8-12) have also reported geographical variations of HBsAg seropositivity within their countries. Among them, the study from China (8) showed a higher positivity of HBsAg in coast areas, comparable with ones from Korea.

These descriptive observations suggest a possibility that sea-related environmental factors are involved in the transmission of HBV. In this case, seafood might be thought as one of possible sources of transmission, because some seafood could be consumed as raw. Interestingly, in the 1960s and 1970s, there were two papers (13, 14) that reported detection of HBsAg in shellfish taken from polluted area and evidence of shellfish to shellfish transmission. Relating to this hypothesis, another important finding of our study was that the HBsAg positivity increased depending on the frequency of eating out, suggesting HBsAg seropositivity might be associated with diet itself or diet-related behavior.

As perinatal and childhood transmission have been generally regarded as important transmission routes in a highly endemic area such as Asia, the hypothesis of the current exposure to some food being involved in the transmission in HBV seems unlikely. However, cohort studies from Korea (6, 15) demonstrated that the HBV infection occurs commonly in adulthood, however most of those infected in their adulthood tended to be transient carriers, whereas those infected in young age tended to be chronic carriers. This finding has been supported by one prospective study from Alaska (16). The prevalence of HBsAg carrier of the present study was determined at a single time point, so transient carriers would have been mixed with chronic carriers.

Fortunately, we had data supporting that there would be a substantial portion of transient carriers, especially among subgroups with a high seropositivity of HBsAg in our study (living in Jeju Island and/or eating out frequently). A report (17) from China showed that chronic HBV infection, which usually starts in early childhood, leads to a lower lipid concentration in adulthood, since the liver plays a fundamental role in lipid metabolism. In their study, the blood concentration of lipid was significantly lower among healthy HBsAg carriers, as compared with than among non-carriers. Our study subjects also showed the same tendency (data not shown). However, in case of the subgroups with a high prevalence of HBsAg, the mean concentrations of cholesterol in carriers and non-carriers were similar and that of triglyceride was even higher among carriers than among non-carriers. This suggests

that a substantial portion of carriers from these subgroups with a high seropositivity of HBsAg would have been recently infected via an unknown route of transmission, which might currently exist among these subgroups. The relationship between the carrier state and lipid concentrations will be analyzed in detail in our forthcoming paper.

Surprisingly, this study demonstrated a very consistent positive association between HBsAg seropositivity and socioeconomic status, particularly the household income level. This relationship was observed in both males and females, and even after stratification by urban-rural residency or administrative area.

Until now, the HBV infection has been also known to be more common in underdeveloped or developing countries than developed countries like other infectious diseases. Within a country, studies from U.S.A. (18), Italy (9), and Jordan (12) have indicated that the HBV infection is associated with lower socioeconomic status. It has been attributed to a crowded home environment and/or poor environmental or personal hygiene. In addition, since those with a higher socioeconomic status tend to receive vaccination more often, the positive association shown in this study is certainly an unexpected one.

As far as we know, this is the first study reporting a positive association between HBsAg seropositivity and socioeconomic status on an individual basis, although there is an ecological data (17) on 81 villages in rural China showing a positive correlation between the prevalence of HBsAg and the mean lipid concentration. They interpreted that differences in mean lipid concentration were probably associated with differing degrees of urbanization and industrialization, which could be another index of socioeconomic status.

We believe that it is likely true, considering the random nature of sampling of study subjects and the striking consistency of our findings. If the negative findings of other countries were also true, the association between HBV infection and socioeconomic status may not simply be a function of a crowded home environment and/or poor environmental or personal hygiene. This may reflect a relationship with other cultural factors. For example, there may be certain factors that are common in those with a high socioeconomic status in some countries but common to lower classes in other countries.

There would be a possibility that persons with higher income may be more exposed to the known exposure routes, such as transfusion, medical procedures, drug use, or sexual behavior, than those with lower income. We could not totally exclude this possibility because information on these factors was not examined in this study. However, as far as we know there has been no report suggesting this possibility in any country as well as Korea and it would be difficult to think that these known risk factors are common in the high socioeconomic class only in Korea. Our data have demonstrated that the unknown factor related with the high income should be general because a positive association appeared across most strata stratified by sex, urban-rural residency, or admin-

istrative area. In this case, we could think of the relation with nutrition or diet once again. In particular, raw seafood is generally an expensive food in Korea and more accessible to persons with high income. On the other hand, there is an interesting paper (19) on the epidemiology of non-A, non-B hepatitis in the United States, comparable to ours, which showed that individuals with non-A, non-B hepatitis who had clear parenteral exposures had a lower socioeconomic status, but those without a history of parenteral exposures (possibly associated with personal contact, ingestion of raw shellfish, or no known risk factor) had a higher socioeconomic status.

Despite the limitation in interpretation due to the cross-sectional nature of the study design, our results imply the possibility of existence of another transmission route, probably related to diet. Although the HBV vaccination program has resulted in a decline of HBV infection in Korea, we must uncover other possible transmission routes in order to further prevent HBV infection.

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