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# Trends in the seroprevalence of hepatitis B surface antigen in the South Korean population

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SUMMARY

*Background:* Trends in hepatitis B virus (HBV) infection are important in evaluating the effectiveness of the recommended routine vaccination of infants and adolescents.
*Methods:* The prevalence of HBV infection was determined in a representative sample of the Korea National Health and Nutrition Examination Survey for 1998 ($n$ = 9771) and 2009 ($n$ = 8304). Participants aged ≥10 years were tested for the hepatitis B surface antigen (HBsAg).
*Results:* The overall age-adjusted HBsAg seroprevalence was 4.6% (95% confidence interval (CI) 4.2–5.0%) in 1998 and 3.2% (95% CI 2.9–3.6%) in 2009, which represents a relative decrease of 30.4% between the two survey populations ($p < 0.05$). The prevalence of HBsAg decreased among persons 10–19 years of age (from 2.2% to 0.3%), 20–29 years of age (from 5.4% to 2.5%), 30–39 years of age (from 6.1% to 4.3%), 40–49 years of age (from 5.1% to 4.7%), and 50–59 years of age (from 5.3% to 3.7%). HBsAg seroprevalence did not decrease among persons ≥60 years of age (2.7% vs. 2.9%).
*Conclusions:* These data show a decline in HBsAg seroprevalence, primarily due to the dramatic decrease in adolescents and younger adults.


## 1. Introduction

Hepatitis B virus (HBV) infection remains a major public health burden in many parts of the world, especially in high prevalence areas such as the Asia-Pacific region. It is estimated that more than 2 billion people worldwide have been infected with HBV. Of these people, approximately 360 million individuals (6% of the world population) are chronically infected and are at risk of serious illness and death, mainly from liver cirrhosis or hepatocellular carcinoma. Mathematical modeling for the year 2000 estimated the yearly number of deaths from HBV-related diseases to be approximately 600 000 worldwide.[1] Because, HBV is most commonly spread from mother to child at birth or from person to person in early childhood in highly endemic areas,[2–4] universal infant vaccination is the single most effective measure in preventing the transmission of HBV. In 1992, the World Health Organization recommended that all countries implement universal HBV vaccination by 1997.[5] Most countries have incorporated universal HBV vaccination into their national infant immunization programs. As of 2008, 177 (92%) of the 193 World Health Organization member states had initiated HBV vaccination programs.[6] Before the introduction of the HBV vaccine in Korea, the prevalence of HBV was up to 10% in the general population.[7] The first national HBV vaccination program began in 1985 for newborn infants whose mothers were HBV surface antigen (HBsAg) carriers, and the national universal vaccination program was launched in 1995.

As the majority of people infected with HBV do not develop clinical disease, seroepidemiological studies provide a more comprehensive picture of the distribution of this infection compared to acute disease surveillance. Trends in HBV infection are important in evaluating the effectiveness of the recommended routine vaccination of infants and adolescents along with adults at high risk of infection. To assess Korean trends in the prevalence of HBV and to provide the first nationally representative analysis of the impact of the nationwide universal vaccination program, we compared the prevalence of HBV infection among the Korea National Health and Nutrition Examination Survey (KNHANES) participants in 1998 to the prevalence among participants in the 2009 survey.

## 2. Methods

### 2.1. Sample population

KNHANES is a series of cross-sectional, national health and nutrition surveys designed to provide representative prevalence estimates for a variety of health measures and conditions and is conducted by the Korea Centers for Disease Control and Prevention. The survey design is a complex, stratified, multi-stage

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probability sampling of the civilian, non-institutionalized Korean population. The procedures used to select the sample and conduct the interview and examination have been specified elsewhere.[8] The survey included an interview to obtain information on health history, health behaviors, and risk factors, and a subsequent health examination was performed at a mobile examination center.

Our analyses include data from 1998 (KNHANES 1998) and 2009 (KNHANES 2009). Starting with KNHANES 1998, serum samples from participants aged ≥10 years were tested for HBsAg (electrochemiluminescence immunoassay; Roche Diagnostics, Switzerland), but antibodies to hepatitis B core antigen (anti-HB) and hepatitis B surface antigen (anti-HB) were not included in the KNHANES protocol. In KNHANES 1998, 10 876 individuals aged ≥10 years were sampled, and 9771 individuals participated in the seroepidemiological survey; the response rate was 89.8%. In KNHANES 2009, 9231 individuals aged ≥10 years were sampled, and 8304 individuals completed the survey; the response rate was 90%. Sample weights were used to account for the differential probabilities of selection and nonresponse[9] and were included in the estimation process for all analyses. Prevalence estimates were age-adjusted by the direct method, using the age groups from the 2005 Korean Census population for comparisons across subgroups and between surveys. Informed consent was obtained from all participants, and the Institutional Review Board of the Korea Centers for Disease Control and Prevention approved the protocol.

### 2.2. Data analyses

Demographic variables (age, sex, and area of residence (urban or rural)), education, marital status, and family income were considered as covariates. Monthly family income was calculated by household income divided by the number of household members and grouped into 4 categories. Weighted frequencies and cross-tabulations were computed to represent the Korean civilian, non-institutionalized population and to account for over-sampling and non-response to the interview and medical examination. Sample weights were included in all estimations. Multiple logistic regression of the KNHANES 2009 dataset was used to estimate the odds ratios (OR) of HBsAg seroprevalence while controlling for the covariates listed above. Prevalence estimates of HBsAg for some subgroups, as noted in the tables, are based on a small number of persons with positive results and may be unstable. Differences in HBsAg seroprevalence between the surveys were considered to be statistically significant if the two-sampled $t$-test had a $p$-value of less than 0.05.[10] Statistical hypotheses were tested at the $p < 0.05$ level of significance.

## 3. Results

In 2009, the seroprevalence of HBsAg among participants aged ≥10 years was 3.2% (95% confidence interval (CI) 2.8–3.6%; Table 1). The seroprevalence was higher among males than among females (3.5% vs. 2.9%; $p < 0.05$). The prevalence of HBsAg was considerably lower among teenagers (0.3%) than in the other age groups. Prevalence increased rapidly with increasing age, peaking in the 40–49 years age group (4.7%), and decreased in the 50–59 years age group (3.7%) and among persons aged ≥60 years (2.9%). In comparison with persons who were married, those who had never been married had a decreased prevalence of infection. However, there was no difference between groups according to level of education, family income, or area of residence.

Using the 2005 Korean Census civilian, non-institutionalized population aged ≥10 years as the standard, the overall age-adjusted HBsAg seroprevalence was 4.6% (95% CI 4.2–5.0%) in 1998 and 3.2% (95% CI 2.9–3.6%) in 2009, a relative decrease of 30.4% between the two surveys ($p < 0.05$; Table 2). There was a 28.8% decrease in males and a 30% decrease in females, and these decreases were statistically significant. In addition, seroprevalence

**Table 1**
Weighted hepatitis B virus surface antigen seroprevalence among persons aged 10 years and older in KNHANES 2009

| | Sample size | Prevalence, % (95% CI) | Unadjusted OR (95% CI) | Adjusted OR[a] (95% CI) |
|---|---|---|---|---|
| Overall | 8304 | 3.2 (2.8–3.6) | | |
| Sex | | | | |
| Female | 4580 | 2.9 (2.4–3.4) | 1 | 1 |
| Male | 3724 | 3.5 (3.0–4.2) | 1.36 (1.06–1.74) | 1.30 (1.01–1.67) |
| Age group, years | | | | |
| 10–19 | 1203 | 0.3 (0.09–0.8)[b] | 1 | 1 |
| 20–29 | 930 | 2.5 (1.8–3.5) | 9.36 (2.96–29.6) | 8.05 (2.48–26.17) |
| 30–39 | 1385 | 4.3 (3.5–5.5) | 16.53 (5.37–50.91) | 12.80 (3.83–42.77) |
| 40–49 | 1475 | 4.7 (3.8–5.9) | 17.98 (5.85–55.23) | 14.22 (4.25–47.60) |
| 50–59 | 1218 | 3.7 (2.7–4.9) | 13.71 (4.39–42.82) | 11.14 (3.31–37.53) |
| ≥60 | 2093 | 2.9 (2.2–4.0) | 10.88 (3.46–34.16) | 8.87 (2.62–30.04) |
| Marital status (participants aged ≥20 years) | | | | |
| Married/cohabiting | 5125 | 4.0 (3.5–4.6) | 1 | 1 |
| Divorced/separated/widowed | 977 | 3.5 (2.4–5.0) | 0.85 (0.57–1.28) | 1.05 (0.67–1.65) |
| Never married | 999 | 2.7 (2.0–3.7) | 0.67 (0.47–0.94) | 0.58 (0.38–0.88) |
| Education (participants aged ≥20 years) | | | | |
| Less than high school | 2722 | 3.2 (2.5–4.0) | 1 | 1 |
| High school | 2448 | 3.4 (2.8–4.2) | 1.08 (0.79–1.47) | 1.01 (0.68–1.48) |
| College or higher | 1881 | 4.5 (3.7–5.4) | 1.41 (1.03–1.93) | 1.26 (0.84–1.90) |
| Missing | 50 | | | |
| Family income | | | | |
| Low | 1618 | 3.2 (2.4–4.3) | 1 | 1 |
| Mid-low | 1895 | 3.2 (2.5–4.1) | 1.00 (0.67–1.50) | 0.94 (0.61–1.44) |
| Mid-high | 2350 | 2.7 (2.2–3.5) | 0.86 (0.58–1.27) | 0.76 (0.50–1.17) |
| High | 2356 | 3.8 (3.1–4.6) | 1.22 (0.84–1.76) | 0.98 (0.65–1.48) |
| Missing | 85 | | | |
| Area of residence | | | | |
| Urban | 6282 | 3.2 (2.8–3.6) | 1 | 1 |
| Rural | 2022 | 3.4 (2.6–4.4) | 1.05 (0.77–1.43) | 1.06 (0.77–1.45) |

KNHANES, Korea National Health and Nutrition Examination Survey; CI, confidence interval; OR, odds ratio.
[a] Adjusted for sex, age, marital status, education attainment, family income, and area of residence.
[b] Estimate based on <10 individuals with positive samples.

**Table 2**
Changes in weighted hepatitis B virus surface antigen seroprevalence among persons aged 10 years and older between 1998 and 2009

| | 1998 | | 2009 | | |
|---|---|---|---|---|---|
| | Sample size | Prevalence, % (95% CI) | Sample size | Prevalence, % (95% CI) | Difference (95% CI) |
| Overall[a] | 9771 | 4.6 (4.2–5.0) | 8304 | 3.2 (2.9–3.6) | 1.4 (1.3–1.5)[b] |
| Age group, years | | | | | |
| 10–19 | 1809 | 2.2 (1.7–2.9) | 1203 | 0.3 (0.09–0.8)[c] | 1.9 (1.8–2.0)[b] |
| 20–29 | 1493 | 5.4 (4.6–6.4) | 930 | 2.5 (1.8–3.5) | 2.9 (2.7–3.1)[b] |
| 30–39 | 1968 | 6.1 (5.2–7.0) | 1385 | 4.3 (3.5–5.5) | 1.8 (1.5–2.1)[b] |
| 40–49 | 1630 | 5.1 (4.3–6.1) | 1475 | 4.7 (3.8–5.9) | 0.4 (0.1–0.7)[b] |
| 50–59 | 1260 | 5.3 (4.3–6.6) | 1218 | 3.7 (2.7–4.9) | 1.6 (1.3–1.9)[b] |
| ≥60 | 1611 | 2.7 (2.0–3.6) | 2093 | 2.9 (2.2–4.0) | 0.2 (0–0.4) |
| Sex by age group, years | | | | | |
| Male | | | | | |
| All ages[a] | | 5.2 (4.8–5.7) | 3724 | 3.7 (3.1–4.3) | 1.5 (1.3–1.7)[b] |
| 10–19 | 917 | 1.9 (1.3–2.8) | 624 | 0.3 (0.1–1.2)[c] | 1.6 (1.5–1.7)[b] |
| 20–29 | 659 | 6.9 (5.6–8.6) | 432 | 2.9 (1.9–4.5) | 4.0 (3.6–4.4)[b] |
| 30–39 | 923 | 6.2 (5.0–7.5) | 587 | 4.8 (3.6–6.5) | 1.4 (0.9–1.9)[b] |
| 40–49 | 775 | 6.3 (5.1–7.9) | 631 | 5.8 (4.4–7.6) | 0.5 (0–1.0) |
| 50–59 | 575 | 6.4 (4.8–8.4) | 540 | 4.4 (3.1–6.3) | 2.0 (1.4–2.6)[b] |
| ≥60 | 665 | 2.6 (1.7–4.1) | 910 | 2.6 (1.6–4.2) | 0 |
| Female | | | | | |
| All ages[a] | | 4.0 (3.6–4.4) | 4580 | 2.8 (2.3–3.3) | 1.2 (1.1–1.3)[b] |
| 10–19 | 892 | 2.5 (1.8–3.5) | 579 | 0.2 (0.04–1.0)[c] | 2.3 (2.2–2.4)[b] |
| 20–29 | 834 | 4.1 (3.1–5.3) | 498 | 2.0 (1.2–3.4)[c] | 2.1 (1.8–2.4)[b] |
| 30–39 | 1045 | 6.0 (4.9–7.4) | 798 | 3.8 (2.7–5.4) | 2.2 (1.8–2.6)[b] |
| 40–49 | 855 | 3.9 (2.9–5.2) | 844 | 3.7 (2.6–5.2) | 0.2 (-0.1–0.5) |
| 50–59 | 685 | 4.2 (3.0–5.8) | 678 | 2.8 (1.8–4.5) | 1.4 (1.1–1.7)[b] |
| ≥60 | 946 | 2.8 (2.0–4.0) | 1183 | 3.1 (2.1–4.6) | 0.3 (0–0.6) |

CI, confidence interval.
[a] Age-adjusted using the 2005 Korean Census civilian, non-institutionalized population as the standard.
[b] $p < 0.05$ determined by $t$-test evaluating difference across surveys.
[c] Estimate based on < 10 individuals with positive samples.

of HBsAg decreased significantly in all age groups, except in participants aged ≥60 years. In particular, the prevalence decreased dramatically in teenagers with a relative decrease of 86.4%, and in the 20–29 years age group with a relative decrease of 53.7% (Figure 1).

## 4. Discussion

The KNHANES is the only population-based survey that provides nationally representative estimates of the prevalence – and, therefore, the lifetime risk – of HBV infection. The two surveys described here demonstrate a decrease in the seroprevalence of HBsAg in Korea of 30% in persons aged ≥10 years over the 11-year interval. The change in HBsAg seroprevalence is consistent with data from previous reports from around the world, which have shown the prevalence of HBsAg or HBV infection to have declined significantly since the introduction of hepatitis B vaccination programs, especially in children and adolescents.[11–13]

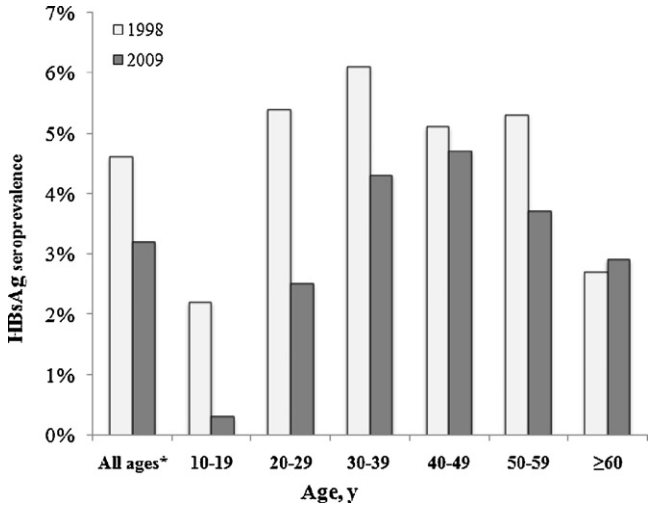


**Figure 1.** Hepatitis B virus surface antigen seroprevalence by age in 1998 and 2009 (the percentage of persons is weighted; *age-adjusted using the 2005 Korean Census civilian, non-institutionalized population as the standard).

Because HBV is a lifetime infection, any increases or decreases in HBsAg seroprevalence are expected to be seen first in younger persons. In adolescents and younger adults, HBsAg seroprevalence is a cumulative measure of recent exposures. The most dramatic finding of this study is the decrease in HBsAg prevalence among teenagers and the 20–29 years age group. The HBsAg prevalence among participants aged 10–19 and 20–29 years decreased by 86% and 54%, respectively. The decrease in HBsAg seroprevalence in these groups provides biological evidence supporting findings from a national survey that showed approximately 79.7% of neonates born after 1983 and 98.9% of neonates born after 1990 received the HBV vaccine.[14] The first domestic plasma-derived HBV vaccine became available in Korea in 1982, and HBV vaccination has been recommended for all neonates since 1983. A national HBV vaccination program for school-aged children was launched in Korea in 1988, and the HBV vaccination was incorporated into the national vaccination guidelines in 1991.[15] The dramatic decline in HBV infection that was found in this study may be related to these immunization efforts.

In addition, a decrease in HBsAg seroprevalence in adults is not unexpected, due to other possible contributing factors, such as the policy that reduces horizontal transmission in the home and safer injection practices that reduce nosocomial transmission. The HBV vaccine is also recommended for high-risk adult groups (e.g., healthcare workers, drug users, people who live with chronically infected persons, chronic hemodialysis patients, HIV-infected patients, and other immunocompromised persons). Despite the substantial progress in preventing HBV infection in adolescents, this study confirms the ongoing high prevalence of HBV infection among adults and the consequent high risks of HBV transmission

and chronic sequelae. This finding emphasizes the need to improve screening programs and other efforts to identify chronically infected persons, most of whom remain asymptomatic until they develop cirrhosis or end-stage liver disease. Programs to prevent the long-term consequences of HBV infection, including screening and antiviral drug treatment, should be developed and expanded to reach those at risk of developing cirrhosis and liver cancer.[16]

A major strength of the present study is that the data are representative of the Korean population and were collected using standardized measurements. However, there are also a number of limitations. Because anti-HBs and anti-HBc tests were not included in the KNHANES protocol, only current HBV infections could be examined, not past HBV infection or vaccine-induced immunity. Also, HBV vaccinations and histories of HBV disease are not recorded in KNHANES; therefore, we do not know the effect of vaccination on HBsAg seropositivity. Another limitation is that the survey participants were sampled only from the non-institutionalized Korean population, excluding incarcerated persons and homeless persons, among whom HBV prevalence is known to be high.[17] Therefore, the overall HBsAg prevalence is underestimated.

In conclusion, these findings from a nationally representative sample provide the most up-to-date prevalence estimates of HBsAg seropositivity in the Korean population. The HBsAg seroprevalence in persons aged $\geq$10 years in 2009 was 3.2%, which is a significant decrease from 4.6% in 1998, though this prevalence still illustrates the remaining high burden of HBV infection. The decreased HBsAg seroprevalence was primarily due to a dramatic decline in adolescents and younger adults. The ability to monitor HBsAg seroprevalence using KNHANES is important for improving HBV prevention strategies, such as those related to ongoing HBV vaccinations. As we continue to report decreases in HBV infection, especially in younger persons, we will see a concomitant decrease in HBV-related morbidity and associated medical costs.

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*Conflict of interest:* The author has no competing interests to declare.

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