

## Hepatitis B infection among adults in the philippines: A national seroprevalence study

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### Abstract

**AIM:** To determine the prevalence of hepatitis B surface antigen (HBsAg) seropositivity among adult Filipinos.

**METHODS:** Testing for HBsAg was performed on serum samples from persons aged  $\geq 20$  years old who participated in the National Nutrition and Health Survey (NNHeS) conducted in 2003. Information on age, sex, marital status, educational attainment, employ-

ment status, and income were collected. For this study, marital status was classified as never married or otherwise (*i.e.*, married, divorced, separated, widowed); educational attainment was classified as high school graduate or below or at least some tertiary education; and employment status was classified as currently employed or currently unemployed. Annual income was divided into 4 quartiles in Philippine pesos (PhP): Q1,  $\leq$  PhP 53064; Q2, PhP 53065-92192; Q3, PhP 92193-173387; and Q4,  $\geq$  PhP 173388. Prevalence estimates were weighted so that they represented the general population. Social and demographic factors were correlated with HBsAg seropositivity. Multivariate analysis was used to determine independent predictors of HBsAg seropositivity.

**RESULTS:** A total of 2150 randomly selected adults, 20 years and over, out of the 4753 adult participants of NNHeS were tested for HBsAg. The HBsAg seroprevalence was 16.7% (95%CI: 14.3%-19.1%), which corresponded to an estimated 7278968 persons infected with hepatitis B. There was no significant difference between males and females (17.5% *vs* 16.0%;  $P = 0.555$ ). This corresponded to an estimated 3721775 men and 3557193 women infected with hepatitis B. The HBsAg seroprevalence peaked at age 20-39 years old, with declining prevalence in the older age groups. The only independent predictor of HBsAg seropositivity was the annual income, with persons in the highest income quartile being less likely to be HBsAg positive (age-adjusted OR = 0.51; 95%CI: 0.30-0.86) compared to subjects in the lowest income quartile. Sex, marital status, educational attainment, and employment status were not found to be independent predictors of HBsAg seropositivity.

**CONCLUSION:** The high HBsAg seroprevalence among adults in the Philippines classifies the country as hyper-endemic for HBV infection and appears unchanged over the last few decades.

**Key words:** Prevalence; Hepatitis B; Survey; Philippines; Asia

**Core tip:** Chronic hepatitis B has a significant public health impact in the Philippines because it is a common cause of end stage liver disease and is the leading cause of hepatocellular carcinoma, the latter being the fourth leading cancer and the second leading cause of cancer death in the country. However, an accurate estimate of the national prevalence of hepatitis B infection in the Philippines is lacking. To determine the national prevalence of hepatitis B infection in the Philippines, testing for hepatitis B surface antigen was undertaken on serum samples collected from subjects included in the National Nutrition and Health Survey.

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## INTRODUCTION

Chronic hepatitis B (CHB) remains to be a significant public health burden affecting 400 million people worldwide, and is most prevalent in the Asia Pacific region<sup>[1]</sup>. The disease is estimated to account for 30% of cirrhosis and 53% of hepatocellular carcinoma (HCC) cases worldwide. As such, it is responsible for a staggering half a million deaths every year from hepatitis B virus (HBV)-related cirrhosis and HCC<sup>[2]</sup>.

The Philippines is considered an endemic country for hepatitis B. Chronic hepatitis B has a significant public health impact in the Philippines because it is a common cause of end stage liver disease and is the leading cause of HCC<sup>[3,4]</sup>, the latter being the fourth leading cancer and the second leading cause of cancer death in the country<sup>[5]</sup>. However, an accurate estimate of the national prevalence of hepatitis B infection in the Philippines is lacking. Although many prevalence studies have been done earlier, they either included small sample sizes, or were done only in select populations (*i.e.*, overseas employment applicants, certain ethnic groups, limited locality, institutional, *etc.*)<sup>[6-9]</sup>. Accurate prevalence estimates in the general population are important in the control of HBV infection and its complications, and may especially be instrumental in shaping health policies on primary and secondary prevention of this infection.

To determine the national prevalence of hepatitis B infection in the Philippines, testing for hepatitis B surface antigen (HBsAg) was undertaken on serum samples collected from subjects included in the National Nutrition and Health Survey (NNHeS).

## MATERIALS AND METHODS

### NNHeS and data collection

NNHeS was conducted in 2003 as a collaborative effort among the Food and Nutrition Research Institute of the Department of Science and Technology (FNRI-DOST), the department of health, and fourteen medical specialty associations in the country. The NNHeS was conducted in conjunction with the 6<sup>th</sup> National Nutrition Survey of the FNRI-DOST. The study protocol was approved by the Technical Committee and Ethical Review Board of the DOST. Studies on the prevalence and risk factors of atherosclerosis-related diseases and metabolic syndrome have been published using the data from the survey<sup>[10,11]</sup>.

The survey utilized the National Statistics Office Master Sample with household listing taken from the Family Income and Expenditure Survey. A stratified multi-stage sampling design was employed to represent each of the 17 regions in the country. The sampling method utilized the “Barangay” which is the basic political unit in the Philippines that serves as the primary planning and implementing unit of government policies and programs and which is created out of a contiguous territory with at least 2000 inhabitants<sup>[10]</sup>. The first stage involved the selection of the Primary Sampling Units (PSUs) in a barangay or contiguous barangays with at least 500 households with probability proportional to the estimated number of households. The second stage involved selection of Enumeration Areas (EAs) within sampled PSUs with 150-200 households serving as the Secondary Sampling Units. The last stage was the selection of housing units within the sampled EAs which served as the ultimate sampling unit. As such, the household was considered as a cluster in which all the units became part of the survey. The clinical component of the NNHeS covered only one of the four replicates of the Master Sample and 25% of the households. A replicate was a sub-sample that possessed the properties of the full master sample such that each replicate was able to generate national level estimates of adequate precision. Adults 20 years and over served as participants of the study.

Information on age, sex, marital status, educational attainment, employment status, and income were collected. For this study, marital status was classified as never married or otherwise (*i.e.*, married, divorced, separated, widowed); educational attainment was classified as high school graduate or below or at least some tertiary education; and employment status was classified as currently employed or currently unemployed. Annual income was divided into 4 quartiles in Philippine pesos (PhP): Q1, ≤ PhP 53064; Q2, PhP 53065-92192; Q3, PhP 92193-173387; and Q4, ≥ PhP 173388 according to categories of income used in a World Health Organization publication on non-communicable diseases and socioeconomic inequalities<sup>[12]</sup>.

### Laboratory methods

HBsAg testing was performed on serum samples col-

**Table 1** Prevalence of hepatitis B surface antigen positivity according to demographic characteristics *n* (%)

	HBsAg positive	95%CI	P value
All adults	2150 (16.7)	14.3-19.1	
Sex			0.555
Females	1194 (16.0)	13.0-18.9	
Males	956 (17.5)	14.1-20.8	
Marital status <sup>1</sup>			0.177
Never married	261 (19.3)	13.6-25.0	
Otherwise	1883 (16.0)	13.5-18.4	
Educational attainment <sup>1</sup>			0.021
High school	1412 (18.6)	15.5-21.7	
At least some tertiary	720 (14.6)	11.3-18.0	
Employment status			0.189
Unemployed	1077 (15.4)	12.0-18.8	
Employed	1073 (17.5)	14.4-20.7	
Income <sup>1</sup>			0.003
Q1	484 (20.6)	13.2-18.4	
Q2	564 (19.2)	14.6-23.8	
Q3	566 (16.8)	12.1-21.5	
Q4	502 (11.3)	7.0-15.6	

<sup>1</sup>Missing data. HBsAg: Hepatitis B surface antigen.

lected from adults aged 20 years or over. Samples were tested using the AxSym HBsAg (V2) assay from Abbott Laboratories. Samples with values less than 2.00 were considered non-reactive by the AxSym HBsAg (V2) assay and those with values greater than or equal to 2.00 were considered reactive.

### Statistical analysis

Data set was checked for inconsistencies and values were validated. Estimates of prevalence were weighted so that they represented the national population of the Philippines in 2003. Sampling weights were also applied to account for the selection of a subsample of subjects on whom HBsAg testing was performed. Weighted prevalence by age, sex and demographic variables were computed using Stata Release 11. Age-adjusted multivariate analysis was done to determine independent predictors of HBsAg positivity. A *P* value of < 0.05 was considered statistically significant.

## RESULTS

A total of 2150 randomly selected adults, 20 years and over, out of the 4753 adult participants of NNHeS were tested for HBsAg. The prevalence of HBsAg seropositivity among adults in the Philippines was 16.7% (95%CI: 14.3%-19.1%), which corresponded to an estimated 7278968 persons infected with hepatitis B (Tables 1 and 2).

The prevalence of HBsAg seropositivity was higher among men compared to women but the difference was not statistically significant (17.5% *vs* 16.0%, *P* = 0.555) (Table 1). This corresponded to an estimated 3721775 men and 3557193 women infected with hepatitis B (Table 2). The prevalence of HBsAg seropositivity according to various age groups is shown on Table 2. HBsAg seropositivity was highest among the 20-39 age group and it was

lower in the older age groups. Table 1 shows the prevalence of HBsAg seropositivity according to the other demographic variables. A significantly higher prevalence of HBsAg seropositivity was observed among those with an educational attainment of high school or less compared to those with at least some tertiary level of education (18.6% *vs* 14.6%, *P* = 0.021). The prevalence of HBsAg seropositivity was also statistically different among the different income groups with the highest prevalence of HBsAg seropositivity observed among those belonging to the lower annual income quartiles (Q1 = 20.6% *vs* Q2 = 19.2% *vs* Q3 = 16.8% *vs* Q4 = 11.3%, *P* = 0.003). While HBsAg seropositivity was more prevalent among those who were never married and those who were employed, the differences were not statistically significant. However, on multivariate analysis, only the annual income was found to be independently predictive of HBsAg seropositivity. Those belonging to the highest income quartile (Q4) were less likely to be HBsAg seropositive (age-adjusted OR = 0.51; 95%CI: 0.30-0.86) compared to those in the lowest income quartile (Q1) (Table 3).

## DISCUSSION

This study shows that the prevalence of HBsAg seropositivity in the Philippines remains in the hyperendemic range at 16.7%, translating to an estimated 7.3 million adult Filipinos infected with HBV. Earlier studies have placed the prevalence of HBV infection to be between 4% to 18%<sup>[6-9]</sup>. A study done in 1986 from 4 rural villages in the country showed a prevalence of 9%-15%, with two peaks observed in the 3-4 and 30-40 year-old age groups<sup>[9]</sup>. More recent studies done almost 20 years later showed that HBsAg seroprevalence in healthy adults appeared to be lower at 5.9% in an urban area<sup>[6]</sup> and 8.4% in a rural area<sup>[7]</sup>. The study done in the urban setting tested archived samples and the study in the rural setting only evaluated persons in a single town within a province. Therefore, both studies do not represent the general population. A study on blood donors and applicants for overseas employment likewise showed a lower prevalence estimate at 4.2% for both groups<sup>[8]</sup>. It is interesting to note that studies that looked at archived serum from “healthy” volunteers and blood donors have shown much lower rates of HBV infection<sup>[6,8]</sup>. The fact that blood donors are pre-screened and excluded outright if they report risk factors for blood-borne diseases (*e.g.*, injection drug use, tattoos, *etc.*) and that so-called “healthy” volunteers are generally persons with access to health care and probably have self-selected based on prior knowledge of HBV infection status may account for the discrepancy compared with estimates done in other population groups. The current study was conducted on a large sample size that represented the general adult population in the Philippines and is therefore a more accurate estimate of the prevalence of hepatitis B infection in this population.

The high HBsAg seroprevalence in the Philippines in 2003 is in contrast to other countries in the Asia Pacific

**Table 2** Prevalence of hepatitis B surface antigen seropositivity and population estimates according to age group and gender *n* (%)

Age group	Total			Males			Females		
		95%CI	Estimated number		95%CI	Estimated number		95%CI	Estimated number
20-29	329 (18.1)	13.6-22.6	2580340	170 (19.5)	13.1-25.9	1392647	159 (16.6)	10.5-22.8	1187693
30-39	314 (17.6)	13.2-22.0	1960314	163 (20.2)	13.6-26.8	1137688	151 (14.9)	9.0-20.7	822626
40-49	252 (16.0)	11.2-20.9	1314240	112 (13.4)	7.2-19.7	567308	140 (18.2)	11.4-25.1	746932
50-59	162 (14.3)	9.0-19.5	715781	66 (10.1)	3.2-16.9	265155	96 (17.2)	9.3-25.0	450626
60-69	638 (14.3)	11.4-17.2	443882	267 (17.6)	12.7-22.6	254760	371 (11.9)	8.3-15.5	189122
70 and over	455 (13.6)	10.0-17.3	264411	178 (12.4)	8.1-16.8	104217	277 (14.4)	9.5-19.2	160194

**Table 3** Relative odds of hepatitis B surface antigen positivity among adults by selected demographic variables

	Adjusted OR	95%CI
Sex		
Females	1.00	
Males	1.06	0.76-1.45
Marital status		
Never married	1.00	
Otherwise	0.75	0.48-1.16
Educational attainment		
High school	1.00	
At least some tertiary	0.78	0.55-1.13
Employment status		
Unemployed	1.00	
Employed	1.18	0.85-1.71
Income		
Q1	1.00	-
Q2	0.94	0.59-1.50
Q3	0.82	0.51-1.31
Q4	0.51	0.30-0.86

region where the latest estimates show that the prevalence of HBV infection has already fallen below previous estimates. In Northeast China and South Korea, recent seroprevalence surveys indicate a two- to three-fold decrease in HBsAg seroprevalence in the last 1-2 decades<sup>[13,14]</sup>. Both countries adopted universal infant vaccination and attributed the declines in HBsAg seroprevalence to the effect of vaccination programs. The current study did not include adults younger than 20 years old and children. Thus, it is not possible to make a complete assessment of the effectiveness of the universal infant vaccination program that was introduced in 1992<sup>[15]</sup>.

The highest prevalence of HBV infection is seen in the 20-39 year-old age group with decreasing HBsAg seroprevalence in the older age groups. This trend is similar to data from other countries in the Asia-Pacific region. While this may be due to older patients with HBV infection dying from cirrhosis and HCC, there is also evidence that even in countries where the predominant mode of HBV transmission is perinatal, HBsAg seroclearance can occur in up to 28% of CHB patients by the time they reach 60 years of age, with a median age of 48 years at the time of HBsAg seroclearance<sup>[16]</sup>. A lower annual income was the only independent predictor of HBsAg seropositivity in our study, and may reflect inequity in the access to health care, including preventive programs such as vaccination, among the different socioeconomic

levels. This is not surprising since studies have shown that patients with lower socioeconomic status are more likely to have delayed and missed vaccinations<sup>[17]</sup>, and are more likely to be ignorant of how HBV is transmitted<sup>[18]</sup>. Moreover, it is also important to note that a low educational status was associated with a higher HBsAg seroprevalence on univariate analysis. The results of the study highlights the importance of a government-subsidized immunization program and a grassroots HBV education program in a nation where the poverty level still hovers around 27%<sup>[19]</sup>.

The continued high HBsAg seroprevalence probably explains why the yearly incidence of HCC for both males (20-21 per 100000) and females (7-8 per 100000) in the Philippines has not changed over the past 20 years<sup>[20]</sup>. The burden of CHB infection expectedly spills over into the public health arena because of the high cost of taking care of one patient with CHB. In Asia, the cost can range from United States Dollar 185-1321 per year for patients with compensated CHB-related cirrhosis, to United States Dollar 49000-66000 for every CHB patient needing a liver transplant<sup>[21,22]</sup>. In countries like the Philippines where there is very little government assistance for healthcare, the cost for CHB care falls squarely on the shoulders of the patients themselves. Therefore, the finding that persons in the lower income brackets are more likely to be infected with HBV makes the impact of this infection on the utilization of healthcare resources in the Philippines even more significant.

Our study has several limitations. We did not include adults younger than 20 years old and children. Thus, the current estimate may consequently not be reflective of the true national HBsAg seroprevalence. However, while universal infant HBV vaccination was first introduced into the national immunization program as early as 1992<sup>[15]</sup>, due to insufficient funds, the program was never fully implemented until January 2007<sup>[23]</sup>. Therefore, since fully funded efforts to curb the perinatal transmission of HBV started only after the study was made, the HBsAg seroprevalence of adults younger than 20 years old and children is not expected to be very different from the estimates in this study. A study evaluating the seroprevalence of HBV in children is needed and is expected to be conducted in the immediate future as the Philippines together with countries in the World Health Organization Western Pacific Region have adopted a region-wide goal to reduce the seroprevalence of HBV in children 5 years



or younger to < 2% by 2012<sup>[24]</sup>. Although the result of this study does not reflect the effects of a successful vaccination program on HBV prevalence rates, it may later serve as a comparison group for adults born after its full implementation. Another study limitation is that testing of the serum antibody to hepatitis B surface antigen and antibody to hepatitis B core antigen were not included. This information could have helped elucidate on the level of HBV exposure and/or success of vaccination. There were missing data for some participants on marital status, educational attainment, and income. However, a reanalysis including only those with complete demographic data did not change the results. Other risk factors for HBV transmission like serology for human immunodeficiency virus, hepatitis C, herpes simplex, and syphilis, history of hemodialysis, of injection drug use, and of blood transfusion as well as sexual histories were not determined and would have helped expound on the epidemiology of HBV infection in the country.

We have shown that HBsAg seroprevalence among adults in the Philippines remains high and appears to be unchanged from previous estimates. That HBV infection is more common among those in the lower income brackets emphasizes the importance of prevention in the control of this infection, especially in a healthcare resource-challenged setting like in the Philippines. The recent gains with universal infant HBV vaccination are a significant step towards bringing down the prevalence of HBV infection. Universal infant HBV vaccination should be part of a government-led multi-sectorial national comprehensive hepatitis B control program that will bring together all the various initiatives on the prevention of HBV infection as well as the management of chronic HBV infection and its consequences.

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## COMMENTS

### Background

Hepatitis B virus (HBV) infection poses a significant health burden in the Philippines. However, an accurate estimate of its national prevalence is lacking. This study aims to determine the prevalence of hepatitis B surface antigen (HBsAg) seropositivity among adult Filipinos.

### Research frontiers

The present study determined the seroprevalence of hepatitis B in the adult general population in the Philippines, which has not been previously performed.

### Innovations and breakthroughs

The findings of the present study show that the seroprevalence of hepatitis B in the adult general population of the Philippines remains high at 16.7%.

### Applications

The findings of high prevalence of hepatitis B infection in the Philippines as well as the association between income and HBsAg seropositivity can be used in the formulation of health policy and programs in hepatitis B control and prevention.

### Peer review

The manuscript reports epidemiological data about HBV infection in Philippines, which could improve the health care in this endemic country. The content is of scientific interest and relevance.

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