HEPATITIS B INFECTION IN RURAL VIETNAM AND THE IMPLICATIONS FOR A NATIONAL PROGRAM OF INFANT IMMUNIZATION

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Abstract. To ascertain hepatitis B virus (HBV) infection rates for Vietnam, we surveyed HBV markers in two districts of Thanh Hoa province. We randomly selected 536 infants (9–<18 months old), 228 children (4 to ≤ 6 years old), 219 adolescents (14 to ≤ 16 years old), and 596 adults (25 to ≤ 40 years old). On questioning, none of those surveyed had received vaccine against HBV. Hepatitis B virus surface antigen (HBsAg) and total HBV core antibody (anti-HBc) were measured in all specimens, and HBV e antigen (HBeAg) in those positive for HBsAg, and HBV surface antibody (anti-HBs) were measured in all others. Current infection (HBsAg+) rates were infants = 12.5%, children = 18.4%, adolescents = 20.5%, and adults = 18.8%. Current or previous infection (HBsAg+, anti-HBc+, or anti-HBs+) increased with age (infants = 19.6%, children = 36.4%, adolescents = 55.3%, adults = 79.2%). Rates of HBeAg among those HBsAg+ were infants = 85.1%, children = 88.1%, adolescents = 71.1%, and adults = 30.4%. The epidemiology of HBV in Vietnam resembles that of many southeast Asian nations before introduction of vaccine. Immunization of newborns will have enormous impact on HBV-related morbidity and mortality there.

INTRODUCTION

Despite the availability of effective vaccines for almost two decades, infection with hepatitis B virus (HBV) remains a major problem in many nations outside Australia, northern Europe, and North America. However, as of October 2002, new priority and lower prices have now enabled 154 nations to include hepatitis B vaccine (HepB vaccine) in their immunization programs (Mayers G, Technical Officer, World Health Organization, Geneva, Switzerland, unpublished data) and prospects for further introduction are excellent.1

In southern and eastern Asia, up to 50% of chronic HBV infection results from perinatal transmission from mother to infant, during or soon after birth.2–4 While some countries use a combined passive/active immunization strategy to prevent perinatal infection, this confers only a marginal increase in protective efficacy over the use of an adequate dose of vaccine alone within a week of birth, which has a protective efficacy of 70–95%.3,5,6 In Taiwan, administration of HepB vaccine (with or without anti-HB immunoglobulin [HBIG] depending on maternal infection status) to all newborns since 1986 has dramatically reduced rates of chronic infection, the incidence of primary hepatocellular carcinoma (PHCC), and cases of acute, fulminant hepatitis B among recipients.7,8 Taiwan’s program demonstrates how careful documentation of baseline9 and follow-up10 data can verify the efficacy and impact of vaccination against HBV.

Vietnam is currently expanding its program of infant vaccination against HBV, and while the results of several large surveys have been published locally, good-quality, population-based data on HBV transmission patterns and carriage rates are currently unavailable. Indeed, the prevalence of HBV infection among almost 100 million people living in the nations of the southern Mekong River region, while assumed to be high, has not been well documented.

Vietnamese data include an age-stratified survey of 1,801 people in one district of the southern province of An Giang, conducted in 1995, in which 11% were positive for hepatitis B virus surface antigen (HBsAg), ranging without a trend across age groups from 6.8% to 17.5% (Hau CH, unpublished data). A survey of 6,911 Hanoi Post Office employees reported 13.6% were HBsAg+, and another survey of 1,780 residents of Hanoi found that 14.4% were HBsAg+. (English abstracts of these Vietnamese references are available upon request.) In 1999, a comprehensive, population-based survey of almost 8,000 residents in one commune of central Binh Dinh province found an overall presumptive carrier rate of 9.9% (11.5% in males and 8.4% in females; 13.8% in males over 20 years of age) (Milne A, The Hepatitis Foundation, Whakatane, New Zealand, unpublished data), and two published surveys of healthy populations in Ho Chi Minh City and Hanoi found that 9–14% were HBsAg+.11,12 Finally, a small survey of children in rural Vietnam reported that 19.5% were HBsAg+.13

While all these data suggest that vaccination against HBV will greatly reduce local rates of PHCC and chronic liver disease, none provide an adequately recent and geographically dispersed baseline for comparison with data that might be collected after vaccine introduction, and none reported on the issue of perinatal transmission. To assist decisions on the strategy for and future evaluation of Vietnam’s nascent HBV immunization program, we conducted a population-based, age-stratified serologic survey of HBV markers among rural Vietnamese.

MATERIALS AND METHODS

The survey took place over a seven-day period in August 1998 in villages in Thanh Hoa province, approximately 150 km south of Hanoi. A total of 1,579 persons from four age groups (536 infants 9 to ≤18 months old [mean = 13.8]; 228 children 4 to ≤6 years old [mean = 5.1]; 219 adolescents 14 to ≤16 years old [mean = 15.0]; and 596 adults 25 to ≤40 years old [mean = 32.9]) were randomly selected using a multi-stage, stratified, random-sampling method, and bled by venisection. When questioned, no participant reported vaccination against HBV before sampling. Informed consent to participate was given by those selected after a community
wide publicity campaign, and the survey was reviewed and approved by the Ethical Standards Committee of the National Institute of Hygiene and Epidemiology (NIHE, Hanoi), by leaders of the participating communities, and by the Vietnam Ministry of Health.

Those sampled live in 18 communes, nine in each of two districts (Quang Xuong: coastal, flat, easily accessible, population density = 1,172/km², population ~270,000; and Ngoc Lac: inland, semi-mountainous, moderately difficult to access, population density = 273/km², population ~130,000). The districts are ethnically distinct, with 99.7% of those sampled in Quang Xuong belonging to the nationally dominant Kinh ethnic group, and 91.6% in Ngoc Lac to other groups (predominantly Muong). The 18 communes sampled were non-randomly selected for their geographic spread, and in each district were divided into three strata (three groups of three communes) for follow-up analyses based on future HepB vaccine introduction strategy. From each of these strata (groups of six communes, three in each district), 30 clusters of households (villages, average population range = 250–1,500) were chosen using a method in which the probability (of selection) is proportional to size (or number of households per village). Because the total population of each stratum was higher in Quang Xuong, there were more clusters there than in Ngoc Lac. Eighty-six villages were selected (some larger ones included two clusters), 46 in Quang Xuong and 40 in Ngoc Lac, and lists of all eligible persons from each of the four age groups were requested from the village chief in each. From these lists, persons of appropriate age were chosen randomly, using a simple random sampling method. The size of the sample and the distribution by age group was limited by cost, but was chosen to enable meaningful comparison of infection rates among infants before and after the introduction of HepB vaccine (soon after this survey), and to achieve a reasonably accurate estimate of the rate of HBV infection among adults. The different survey locations also enabled consideration of influences on the infection rates identified, such as knowledge about HBV infection, ethnicity, education level, access to immunization, penetration of mass media, and other demographic indicators. These variables were assessed in a survey (to be published elsewhere) of female household heads conducted in the same communes just before this one.

On the evening of collection, blood samples were separated and the serum was frozen for subsequent transport to and analysis at the NIHE. All sera were assessed by an enzyme-linked immunosorbent assay (ELISA) (Sanofi Diagnostics Pasteur, Marnes la Coquette, France) for HBsAg and total HBV core antibody (anti-HBc). Samples positive for HBsAg were also tested for HBV e antigen (HBeAg), and HBsAg negative samples were tested for HBV surface antibody (anti-HBs). Repeated thawing and freezing of specimens was avoided. The NIHE participates in the quality assurance program of the World Health Organization (WHO), and quality assurance testing (for HBsAg and anti-HBs only) of all HBsAg+ samples and a random selection of 10% of the HBsAg-samples was undertaken at the Victorian Infectious Diseases Reference Laboratory (VIDRL) in Melbourne, Australia using Murex GE ELISA kits (Murex Biotech Limited, Dartford, Kent, United Kingdom). Sera were transported frozen to this laboratory, which is the regional WHO Collaborating Center for Virus Reference and Research.

All sera were coded with a unique identifier. The lists linking names with codes were destroyed upon completion of testing. The NIHE staff were not blinded as to the age group and location from which each sample derived, but the VIDRL staff were blinded to all demographic indicators and the results at the NIHE at the time of quality assurance testing.

Data were analyzed by computer using EpiInfo, version 6 (Centers for Disease Control and Prevention, Atlanta, GA) and STATA, release 6 (STATA Corporation, College Station, TX). We used chi-square tests and multiple logistic regression (MLR), controlling for the design effect of cluster sampling, to examine the relationships between independent variables and outcomes of interest. Mantel-Haenszel tests for trend were used to assess the relationship between age and infection, and kappa coefficients were used to assess concordance between the two laboratories. Design effects to account for the stratified nature of the sample were calculated and found to be small.

**RESULTS**

The age and sex distribution of those tested are shown in Table 1. There were significantly more males than females (Pearson $\chi^2 = 155$, degrees of freedom [df] = 1, $P < 10^{-5}$) in the total sample due to the predominance of males among the adult group. This was noted particularly in Ngoc Lac and is discussed later in this paper. There was no suggestion of sex inequity among adults in the population sampled.

Recalling that no participant had been vaccinated against HBV, rates of current infection (HBsAg+) and any evidence of current or previous infection (HBsAg+ or HBsAg–anti-HBc+ or HBsAg–anti-HBc–/anti-HBs+), divided by age group and sex, are shown in Table 2. Only one individual (a female infant) was HBsAg+/anti-HBc–. Only 15 individuals (6 infants, 2 children, 1 teenager, and 6 adults) were anti-HBs+ but anti-HBc–. There were 113 HBsAg– persons who were anti-HBc+ but anti-HBs–; 16 of them were infants. The average age of this group of 16 was not less than that of the

**Table 1**

<table>
<thead>
<tr>
<th>Age group</th>
<th>Number</th>
<th>Quang Xuong</th>
<th>Ngoc Lac</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Males</td>
<td>Females</td>
</tr>
<tr>
<td>Infants</td>
<td>536</td>
<td>127 (46.2)</td>
<td>148 (53.8)</td>
</tr>
<tr>
<td>Children</td>
<td>228</td>
<td>69 (53.1)</td>
<td>61 (46.9)</td>
</tr>
<tr>
<td>Teenagers</td>
<td>219</td>
<td>48 (39.3)</td>
<td>74 (60.7)</td>
</tr>
<tr>
<td>Adults</td>
<td>596</td>
<td>232 (49.9)</td>
<td>100 (30.1)</td>
</tr>
<tr>
<td>Total</td>
<td>1,579</td>
<td>476</td>
<td>383</td>
</tr>
</tbody>
</table>

* Values are no. (%)
The prevalence of current infection (HBsAg+), depicted by sex and age group, is shown in Figure 1. The mean rate was 12.5% among infants, 18.4% among children, 20.5% among teenagers, and 18.8% among adults (Table 2). Assuming a natural state of infection of zero and ignoring acute infections at the time of the survey, these results show that approximately two-thirds of the HBV infections resulting in chronic carriage occur by 18 months of age, and most of the rest by age 6.

Multiple logistic regression was used to assess the influence of four variables (age, sex, ethnicity, and district) on current infection rates. The analysis confirmed the influence of age (in comparison with infants, the odds ratio [OR] for current infection among children was 1.6 [adjusted \( P = 0.03 \)], teenagers was 1.8 [adjusted \( P < 0.01 \)], and adults was 1.6 [adjusted \( P = 0.01 \)]). Crude comparisons of rates of current infection between children and teenagers (Pearson \( \chi^2 = 0.32, df = 1, adjusted \ P = 0.57 \)) and teenagers and adults (Pearson \( \chi^2 = 0.32, df = 1, adjusted \ P = 0.57 \)) revealed no increment beyond childhood. A further (crude) analysis found that teenage males were 1.86 times more likely to be HBsAg+ than teenage females (Pearson \( \chi^2 = 3.42, df = 1, P = 0.06 \)). Although the regression suggested no overall difference between the sexes (OR = 1.1, adjusted \( P = 0.37 \)), or across the districts, non-Kinh ethnicity may have been associated with current infection (OR = 1.8, adjusted \( P = 0.13 \)). Although only a trend, this concurs with the higher rates of infection evident among infants (predominantly Muong) in Ngoc Lac (Table 3).

In contrast to the plateau in rates of current HBV infection across the age groups (Figure 1 and Table 2), the rate of any evidence of current or previous HBV infection (Figure 2 and Table 2) shows a monotonous increase for both sexes, as reflected in the mean rates among infants (19.6%), children (36.4%), teenagers (55.3%), and adults (79.2%) (Table 2).

When the influence of same four variables was assessed, MLR suggested a possible difference in any evidence of current or previous infection between the sexes, with a slightly higher risk in males (OR = 1.27, \( P = 0.06 \)). Again, crude analysis showed that this effect was much more apparent in male teenagers, who were 2.2 times more likely than females in this age group to have ever been infected (Pearson \( \chi^2 = 8.31, df = 1, adjusted \ P < 0.01 \)). The effect of age was again apparent (in comparison to infants, the ORs for any evidence of current or previous infection were 2.40 among children [adjusted \( P < 0.001 \), 5.32 among teenagers [adjusted \( P < 0.001 \], and 15.08 among adults [adjusted \( P < 10^{-5} \)]. In addition, crude comparisons across contiguous age groups also revealed that for each increment in age, the rate of current or previous infection increased (between children and teenagers: Pearson \( \chi^2 = 16.0, df = 1, adjusted \ P < 10^{-5} \)) and teenagers and adults (Pearson \( \chi^2 = 46.3, df = 1, adjusted \ P < 10^{-5} \)). No effect of district or ethnicity was evident.

Mantel-Haenszel tests for trend for current and for any evidence of HBV infection demonstrated both to be associated with age (\( \chi^2 = 11.38, df = 3, P = 0.01 \) and \( \chi^2 = 396, df = 3, P < 10^{-5} \), respectively). The results in Figures 1 and 2 suggest that this trend is more obvious for any evidence of than current infection, as would also be expected from the crude analyses.

The rates of HBV infection in the two districts are shown in Table 3 and Figures 3 and 4. Infection was significantly more common among infants in Ngoc Lac than in Quang Xuong (Pearson \( \chi^2 \) for current infection = 7.35, \( df = 1, P < 0.01 \)). Pearson \( \chi^2 \) for any evidence of infection = 5.12, \( df = 1, P = 0.02 \), but these differences had disappeared by childhood and were not evident in the adult group. An interesting trend is visible in Ngoc Lac teenagers, among whom there tended to be more current infections. Building on the data presented earlier on infection rates among teens, within this group data...
not presented showed that Ngoc Lac male teens had a greater risk of infection than females (Pearson $\chi^2$ for current infection = 3.26, df = 1, $P = 0.07$; Pearson $\chi^2$ for any evidence of infection = 6.94, df = 1, $P = 0.008$). A trend in this direction was also present in the same (male teenage) group in Quang Xuong (Pearson $\chi^2$ for any evidence of infection = 2.44, df = 1, $P = 0.12$).

The HBeAg status among sera that were HBsAg+ in both districts by age group and sex is shown in Figure 5. As age increased beyond the child group, a decreasing proportion were HBeAg+ (infants = 85.1%, children = 88.1%, teenagers = 71.1%, adults = 30.4%). This was confirmed with the MLR analysis. The ORs comparing each older age group with the infants decreased from 1.31 (children) to 0.40 (teenagers) and 0.09 (adults) (adjusted $P = 0.06$, 0.06, and $< 10^{-3}$, respectively). Crude comparisons of rates of HBeAg positivity between children and teenagers (Pearson $\chi^2 = 3.82$, df = 1, $P = 0.05$) and teenagers and adults (Pearson $\chi^2 = 21.9$, df = 1, $P = < 10^{-3}$) showed that the presence of HBeAg decreased significantly with age beyond childhood. Males tended to have a lower rate of HBeAg positivity than females (Figure 5; OR = 0.6, adjusted $P = 0.10$), but there was no difference in the rate of HBeAg positivity by district or ethnic group.

There was insufficient serum for all samples sent to the VIDRL to be tested for both HBsAg and anti-HBs. For HBsAg, there were 34 of 268 discordant results (kappa coefficient = 0.73, $P < 10^{-6}$), and for anti-HBs, 15 of 104 (kappa coefficient = 0.71, $P < 10^{-6}$).

**DISCUSSION**

To our knowledge, this is the first population-based, age-stratified serologic survey of HBV infection from Vietnam, Cambodia, or Laos to be published in the international literature. As such, the survey provided valuable assistance to strategic planning for Vietnam’s nascent HBV immunization program, and will provide a useful baseline against which to compare future assessments in this region.

Despite careful attempts to choose a representative sample, there were significantly more males than females surveyed, due to the predominance of males among the adults tested. This occurred because village chiefs sent in their place the male partners of women selected for sampling. Although this sex inequity is unfortunate, the literature does not consistently suggest a sex difference in the prevalence of HBsAg among adults of this age. Indeed, our results are consistent with what was anticipated, and concordance between the NIHE and VIDRL laboratories was very good. Our conclusions are also not altered by the inclusion of the samples yielding atypical results (such as anti-HBc−/anti-HBs+) in the overall analysis, the possible presence of maternally-derived anti-HBc and anti-HBs in some of the youngest infants’ serum,2,14 and the possibility that some of the HBV infections
identified were transient. This is particularly relevant for the adult group in whom acute infection is much less likely because of probable immunity from previous infection.

Differing patterns of risks for and outcomes after HBV infection have been well characterized in many previous serologic surveys. It is established that chronic carriage of HBV is far more likely to result from infection in the perinatal period (90%) than in childhood (20%) or adulthood (0–7%). It is also well recognized that for many reasons, different ethnic or socioeconomic groups within one nation may have differing risks for infection. However, attempts to control HBV by targeting particular groups in communities have generally been acknowledged to fail, and a policy of universal infant immunization has been supported by relevant authorities for at least 10 years.

Although conceivably the result of a birth cohort effect representing improving injection safety and hygiene conditions in Vietnam, the pattern of infection evident across the age groups is consistent with the known epidemiology of HBV infection and was therefore not surprising. There were, however, interesting differences between male and female teenagers. Teenage males, particularly those in Ngoc Lac, tended to be more often currently infected and indeed were more often either currently or previously infected than their female counterparts. These differences in infection rates were absent from the infant and child groups, and less evident among the adults, and are not consistent with any established trend in the literature on HBV epidemiology. They are most likely due to a cohort effect peculiar to males of this age in this location, perhaps resulting from unsafe injections, rough play, or head-shaving. A repeat survey would be needed to pay serious credence to these findings.

Differences in infection rates between infants and children in the two districts are also interesting. They suggest much higher HBV infection rates among infants in Ngoc Lac than in Quang Xuong, but no difference among children, suggesting that children in the latter district have higher interim rates of infection between 18 months and four years of age. For the infants, the higher rate of infection in Ngoc Lac may be explained by differences in maternal infection (for which data from Ngoc Lac are scant in this survey, but for which follow-up data not yet published are suggestive) or injection safety between the two districts. The higher interim rate of infection between the infant and child age groups in Quang Xuong might be explained by its higher population density (more than four times that of Ngoc Lac) or rates of kindergarten attendance (with concomitant risks of horizontally transmitted HBV infection).

The regression analysis showed a trend toward a higher risk of current HBV infection among the non-Kinh ethnic group concentrated in Ngoc Lac. Ethnicity is certainly associated with HBV infection risk, particularly where it is associated with socioeconomic status, and conditions in Ngoc Lac are poorer than in Quang Xuong. Given the relatively uniform, high regional endemicity of HBV among the native peoples of southeast Asia and the Western Pacific, this higher risk in non-Kinh, if real, is more likely due to environmental than inherited risk factors. With respect to other differences between the districts, the preceding household survey identified differences in education level, knowledge about liver disease and HBV, access to a village health worker, mass media and immunization, and in the delivery practices of mothers during confinement. In all cases, these differences favored Quang Xuong, suggesting that the possible higher risk of infection in Ngoc Lac and similar districts may be a real phenomenon.

The data presented enable a robust estimation of the contribution to long-term HBV infection made by perinatal, early childhood, and subsequent infection in rural Vietnam. Although the number of adult females was small, their rate of HBeAg positivity (27.8%) approximates the figure of 28.8% among 2,193 HBsAg+ females 20–39 years old in Taiwan, and similar rates identified in this global region. Based on this figure, the adult female HBsAg positivity rate of 15.8% identified here, and mid-range rates of 80% for perinatal transmission of HBV from HBeAg+ mothers to their infants and 10% from HBsAg+/HBeAg– mothers, we calculate that Vietnamese infants have a 4.7% risk of perinatal HBV infection, with its associated very high risk of chronicity. An additional 7.8% acquire infection during the first 18 months of life, and 5.9% by age 6. After this, infections seem generally not to result in chronic carriage, as expected.
These data concur with the estimates that in highly endemic Asian nations, 20–50% of all chronic HBV infection results from largely preventable perinatal infection.2–4

These findings argue strongly for national neonatal immunization against HBV in all countries in this region, as already implemented in Australia, Thailand, Malaysia, Singapore, and Korea, and as about to commence in China.5–9 New programs of infant vaccination against HBV are commencing in Laos, Cambodia, and Myanmar (Burma), but do not include a neonatal dose at this stage. Existing data regarding use of vaccine alone (without HBIG) is scant, but suggests that a dose of HepB vaccine must be given within a week of birth to confer protection against perinatal infection.6,35,36 Vietnam is currently introducing a birth dose for infants delivered within or close to health facilities. Our results provide a baseline against which to measure the reduction in HBV infection that should result from this, and to compare neonatal vaccination with regimens commencing later in life.

Estimates suggest that 15–25% of chronic HBV carriers will die of PHCC or complications of HBV-induced chronic liver disease, depending on their age at the time of infection,28,37,38 and that in highly endemic countries with a sero-prevalence of 10–15%, HBV is responsible for at least 3% of mortality.3 If the infection rate of 18.5% in Thanh Hoa applies across the nation, then more than 3.5 million Vietnamese are currently at risk of premature death due to HBV infection. Assuming success similar to that achieved in Alaska,39 the Pacific,40,41 Taiwan,42 China,43 Thailand,43 Indonesia,36 Saudi Arabia,37 and The Gambia,45 Vietnam can anticipate a reduction in chronic HBV infection between 0% and 3%. The Taiwanese experience suggests that some benefits in preventing liver disease may even be seen within eight years.7 In addition to benefiting those immunized, it is reasonable to anticipate a reduction in horizontal transmission from immunized infants to their siblings or peers, possibly reducing the rate of HBV infection among older or unimmunized children.40,46 Concurrent improvements in injection safety will have the same effect. Reduction in rates among older children and uninfected adults is even more likely if they are targeted for vaccination.39,40 Although it will only be available free of charge for infants, a public education campaign recommending vaccination against HBV and the wider availability of HepB vaccine in Vietnam may yield a similar effect.

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REFERENCES


32. Lo KJ, Tsai YT, Lee SD, Wu TC, Wang JY, Chen GH, Yeh CL, 1985. Immunoprophylaxis of infection with hepatitis B virus in infants born to HBsAg positive/