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ORIGINAL ARTICLE

Hepatitis B Infection among Korean Americans in Colorado: Evidence of the Need for Serologic Testing and Vaccination

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Background and Aims: **Hepatitis B virus (HBV) infection is significantly higher in Asian American Pacific Islanders (AAPIs) than in the general U.S. population. People chronically infected with HBV not only have the potential for developing cirrhosis and primary hepatocellular carcinoma, but also are potential sources for infecting others. Therefore, early diagnosis of HBV infection can reduce the risk of further transmission of the virus through education and vaccination of high-risk groups. The aim of this study was to screen for current and past HBV infection in this high-risk group.**

Methods: **A community-based participatory study was conducted between 2004 and 2007. A total of 609 Korean Americans (KA) completed HBV blood screening tests in seven Korean churches in Colorado. Current HBV infection (HBsAg), past HBV infection (anti-HBc positive), and HBV susceptibility were measured. Demographic information, including HBV vaccination history on these groups, was obtained.**

Results: **Korean Americans had an almost ten times higher incidence of current (4%) and past HBV infection (41%) than the general U.S population. Older individuals had a higher incidence of past HBV infection and lower immunization rate. The risk of lifetime HBV infection was less among participants younger than 30 (OR: 0.07; 95% CI: 0.02-0.21) and those who self-reported HBV vaccination (OR: 0.12; 95% CI: 0.05-0.29). Variables associated with immunity due to vaccination (anti-HBc negative but positive to anti-HBs) were, age under 30 (OR: 13.86; 95% CI: 4.68-41.05), and self-reported vaccination (OR: 8.06; 95% CI: 3.43-18.92).**

Conclusions: **Our study findings confirm the high prevalence of HBV infection among AAPIs, specifically among AAPIs in regions where AAPIs constitute a small proportion of residents. Given the high incidence of HBV infection among these community-dwelling KA, and that the majority of HBV-infected participants were unaware of their condition, focused HBV screening should be conducted to uncover individuals with HBV.**

Keywords: **Chronic Hepatitis B, Healthcare Disparities, Asian Americans, Vaccination**

Introduction

The greatest health disparity between Asian American Pacific Islanders (AAPIs) and Caucasian Americans is in liver cancer. Liver cancer rates among males are 13 times higher in Vietnamese Americans (VA), 8 times higher in Korean Americans (KA), and 6 times higher in Chinese Americans (CA) than in Caucasian Americans [1, 2]. In China and South Korea, liver cancer ranks 2nd or 3rd among causes of cancer

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deaths, and HBV infection is responsible for 70 to 80% of primary hepatocellular carcinoma (HCC) [3, 4]. A meta-analysis of 32 studies published between 1993 and 1997 reported that a summary odds ratio (OR) was 13.7 for development of HCC among people chronically infected with hepatitis B virus (HBV) [5].

The prevalence of HBV infection in the Asian Pacific region is the highest, with a marked variation ranging from 2% to 20% [6-9] in different countries. Most AAPIs are immigrants from HBV-endemic areas where the HBV infection rate is higher than 8%. AAPIs are at high risk for hepatitis B infection both from vertical transmission during birth and from close daily contact with family members during childhood [10-12]. Moreover, since HBV infection at an early age rarely produces recognizable symptoms of hepatitis, most AAPI carriers of HBV are unrecognized. Consequently, they are at risk for developing liver disease and primary hepatocellular carcinoma and are potential sources for infecting others. A number of epidemiological studies also strongly support the important role of chronic HBV infection early in life for the subsequent development of HCC [13-16]. In addition, it has been estimated that the relative risk of HCC development in chronic HBV carriers is 100 times higher than that in matched controls [17, 18].

Among AAPIs, associations have been reported between chronic hepatitis B infection rates and gender, age, birth country, and vaccination [19-23]. A recent study of AAPIs in California found that the prevalence of chronic HBV infection in AAPIs was 8.9% but was 11.1% among Chinese-born, with a higher rate in males, older participants, and non-vaccinated participants [23]. That study provided data only on Chinese ethnicity while other AAPIs were collapsed into an "other" category. Another study of AAPIs in New York found that the prevalence of chronic HBV infection varied by country of birth, from 21.4% among those born in China to 4.6% among those born in South Korea and 4.3% among those born in other Asian countries [19].

HBV-related disease in AAPIs is an important health problem because HBV infection occurs in 5 to 15% of AAPIs [19-23]. However, these data are from metropolitan cities on the east and west coasts and may not be representative of the sizeable number of AAPIs who live elsewhere. It is important to identify additional susceptible populations: 1) to guide targeted vaccination programs; 2) to screen for chronically infected individuals who are potentially infectious to both household and sexual contacts; and 3) to counsel and refer infected people for medical management. The objectives of this study were to determine the prevalence of hepatitis B serological markers in AAPIs in Colorado and to determine the accuracy of self-reporting of HBV vaccination.

Materials and Methods

Study design

This community-based study for KAs was conducted in partnership with seven Korean American churches from two periods (City A and City B) in Colorado from 2004 to 2007. In order to reach Korean Americans to detect HBV infection, we used a non-traditional setting-churches-to eliminate organizational, systematic, clinical, cultural, and linguistic barriers. The study was a collaborative study with Korean American churches, the Asian Pacific Development Center, the University of Colorado Denver Schools of Nursing and Medicine, and the Colorado Department of Public Health and Environment.

Study population

Korean Americans constitute one of the most rapidly growing subpopulations in the United States. According to census data in 2000, there were 1,076,872 Koreans living in the United States, an increase of 134% since the 1990 census [24]. The South Korean government estimates that over 2 million ethnic Koreans were living in the U.S in 2005 [25]. Korean Americans are the largest Asian American group in Colorado; the 2000 Colorado Census counted 16,395 Korean Americans. Korean cultural norms, language, and health behaviors are different than other Asian ethnic groups. Seventy-seven percent of Koreans go to church and the church has been the center of the Korean-American community serving social, political, and educational as well as religious functions [26, 27]. This study accessed Koreans through their churches, in order to overcome organization, systematic, clinical, cultural, and linguistic barriers. The inclusion criteria were: 1) community-dwelling Korean American men and women; 2) able to come to the church for the blood screening; 3) age between 18 and 70 years old; 4) able to speak or read Korean or English; 5) willing to sign the informed consent form. The study was reviewed and approved by the Colorado Multiple Institutional Review Board and informed consent forms for HBV testing were obtained from the enrolled subjects.

Serological assays

Registered nurses collected the blood specimens (5-10 ml) and delivered to the CDC-certified University of Colorado Hospital laboratory where analyses were done using FDA-approved methods. All our hepatitis assays were run on the analyzer of an Advia Centaur XP Immunoassay System created Bayer Healthcare that is now owned by Siemens Medical Solutions Diagnostics located in Tarrytown New York, USA. Each specimen was tested for hepatitis B surface antigen (HBsAg), antibody to hepatitis B surface antigen (anti-HBs), and antibody to hepatitis B core antigen (anti-HBc). In the first two churches in City A, all specimens were tested for anti-HBs antibody and HBsAg. More than half of these subjects were positive for anti-HBs without a self-reported vaccination history. Based on these findings, we implemented a population-specific sequential serologic test algorithm for high-risk immigrants from HBV-endemic areas and used this algorithm for all subsequent specimens (Figure 1) in City B. First, all specimens were tested for anti-HBs antibody. If those specimens were reactive, the specimens were further tested for core antibody. If they were not reactive, the specimen was tested for surface antigen. Participants who tested positive for HBsAg and negative for anti-HBs were considered to have HBV infection. Their positive status was confirmed by retesting all samples that initially tested positive to HBsAg and subsequently tested positive for anti-HBc. We defined HBV infection (past or current) as the presence of anti-HBc or HBsAg. Vaccine-associated immunity was defined as the presence of anti-HBs without anti-HBc; and susceptibility to HBV infection was defined as the absence of both HBsAg and anti-HBs.

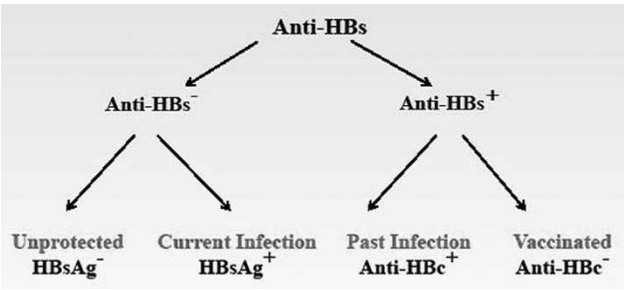

Figure 1. Population-specific sequential serologic test algorithm of HBV.

Data management and analysis

Descriptive statistics were computed on all variables for the full study population and stratified by city and by four infection categories: past HBV infection, vaccinated, chronic HBV infection, and uninfected HBV-susceptible groups. Age was stratified as: under 30 years; 30 to 39; and >40 years. To gain a precise understanding of the relationships between HBV infection status and sociodemographic characteristics and vaccination history, we used a binary logistic regression model. Odds ratios (OR) and 95% confidence intervals (CIs) were calculated for all variables in the model: gender, age, and vaccination history.

Results

Sample characteristics

The serology survey of HBV infection status included 179 KAs in City A and 430 KAs in City B. The mean age was 49 years and 54% were female. Only 8% were younger than 30 years old, reflecting the demographic characteristics of church-goers at Korean churches.

Prevalence of HBV infection and immunization

The prevalence of chronic infection (HBsAg positive) was 24/609 (3.9%); only 4 (16.7%) of the infected participants were aware of their condition. Forty percent of those from City A and 42% from City B were susceptible to infection (absence of both HBsAg and anti-HBs) (Table 1). In City B, 18/430 (4.2%) were HBsAg positive and 231/430 (54%) were HBsAb positive. Among participants who were HBsAg positive and HBsAb positive in City B, 174 (71%) had a past HBV infection while only 70 (29%) had immunity by vaccination. Ninety-four (22%) reported receiving the HBV vaccine and among these, 24 (26%) had a past or current HBV infection.

Table 1. HBV serologic panels for Korean Americans in Colorado.

Subgroups	City A (n=179)	City B (n=430)	Total (n=609)
HBsAg (+)	6 (3%)	18 (4%)	24 (4%)
Anti-HBs (-) & HBsAg (-)	72 (40%)	181 (42%)	253 (41%)
HBsAb (+)	101 (56%)	231 (54%)	332 (55%)
Anti-HBc (+)	-	174 (71%)	-
Anti-HBc (-)	-	70 (29%)	-

Factors associated with HBV infection and immunization

The older subjects had a higher incidence of past HBV infection and were less likely to be immunized (Table 2). Variables, associated with lifetime HBV infection (anti-HBc positive) were older age and no

Table 2. Factors associated with past hepatitis B infection and vaccination among Korean Americans in Colorado.

	Anti-HBc positive cohort (immunity due to past infection)		Anti-HBc negative cohort (immunity due to vaccination)	
Variables	Odds ratio	95% CI	Odds ratio	95% CI
Gender				
Female (reference)				
Male	1.691	0.96-2.98	0.592	0.34-1.04
Age				
Less than 30	0.072***	0.02-0.21	13.86***	4.68-41.05
30 to 49	0.287***	0.15-0.55	3.49***	1.81-6.72
>50 (reference)				
Self-reported vaccination	0.124***	0.05-0.29	8.06***	3.43-18.92

* < 0.05
** < 0.01
*** <0.001

self-report of vaccination. The risk of lifetime HBV infection in people older than 50 years was 14 times higher than that for people younger than 30 years(OR: 0.072; 95% CI: 0.02-0.21), and people who did not self-report vaccination had lifetime HBV infection rates that were 8 times higher than those among people who self-reported vaccination (OR: 0.12; 95% CI: 0.05-0.29). Variables associated with immunity due to vaccination (anti-HBc negative and anti-HBs positive) were age younger than 30 (OR: 13.86; 95% CI: 4.68-41.05) and self-report of vaccination (OR: 8.06; 95% CI: 3.43-18.92). There was no association between current infection and gender, age, or self-report of immunization (P>0.05 in all cases).

Discussion

Among the 609 participants, the prevalence of chronic infection was 3.9% (HBsAg positive). Of the 430 participants in City B, 41% had a past HBV infection and 4% had a current HBV infection, which is approximately 10 times higher than the national average for the general population. According to CDC estimates, 0.1 to 0.5% of the U.S population is currently infected with HBV. However, the 3.9% chronic infection rate found in the current study is consistent with our previous finding (3.4%) [28] and with the recent findings for Koreans living in New York City (4.6%) [19] and Montgomery County, MD (4.0%) in 2007 [21]. It is lower than the rates for other AAPIs such as Chinese-Americans [19-23].

The Third National Health and Nutrition Examination Survey (NHANES III) [29, 30] found a prevalence of 4.9% for serologic markers of current HBV infection among AAPIs; however, the survey used anti-HBc as its measure, which would result in overestimation. Regardless, our findings of 4% for current infection (HBsAg) and 41% for past infection (anti-HBc) are almost ten times higher than the NHANES III report. Studies conducted after implementation of HBV vaccination reported past HBV infection based on a positive test for anti-HBs, which would overestimate past HBV infection by including individuals who tested positive for anti-HBs due to vaccination. Differences in serologic testing might have affected the identification of HBV infections as well as calculation of its prevalence. However, our study included three direct measures: the presence of the virus (HBsAg) and two categories of prior exposure to HB antigens (anti-HBs or anti-HBc). These three direct measures assisted us in differentiating four categories related to HBV infection status: current infection, previous infection, vaccinated, and never infected (unprotected). This study underscores the importance of using a combination of serologic tests (HBsAg, anti-HBs, and anti-HBc) when studying HBV infection patterns among high- risk population like AAPIs from HBV-endemic areas.

Our study suggests that the prevalence of HBV infection among KAs reflects the current prevalence of HBV in their native country. Although the prevalence HBV infection was 8% to 15% before introduction of hepatitis B vaccination in South Korea in the early 1980s [3, 7, 8, 31-34], a national nutritional survey in Korea in 1998 found that the prevalence had dropped to 4.7% among adult men and 4.2% among adult women [35], reflecting the effectiveness of Korea's vaccination program. For persons younger than 20 years old, the prevalence of HBsAg was 2.1% in males and 2.7% in females. However, the earlier study of Koreans in the Eastern U.S between 1988 and 1990 reported 6.1% HBV infection (n=623) in 6,130 unvaccinated Korean-Americans [36], which is somewhat higher than our current data but lower than findings in early 1980s [31-34]. This may reflect the trajectory of decline of HBV in Korean Americans as well as Koreans in South Korea [35]. Our study points to the importance of being mindful of the time of data generation when interpreting HBV data - whether data were collected before or after vaccination programs - and of the ethnicity of AAPIs as more than 85% of AAPIs are either foreign-born or children of foreign-born and many came from HBV-endemic areas [37, 38]; however, prevalence rates of HBV infection and the level of HBV vaccination are varied within Asian countries [6-9].

Our study found that only 70 participants were

immune due to vaccination (anti-HBc negative and anti-HBs positive), which is a very low percentage (16.6%). To the best of our knowledge, this is the first serological report of immunity status of AAPIs that determined the cause of immunity (whether due to past HBV infection or due to vaccination) rather than using self-report data on vaccination. As expected, younger participants were more likely to have been immunized through vaccination, which is in line with population-based studies in Korea [35] and probably reflects governmental efforts at vaccination targeting infants and students in both the U.S. and Korea.

We were unable to use a standard random sampling method because there were no KA listings or directories, and KAs are scattered throughout Colorado. However, there are major limitations with using standard population-based methods in biomedical and epidemiological studies of AAPIs when unique characteristics of the minority population are not considered [26, 27, 37, 39]. For instance, the NHANES III study used a stratified random sampling method that could skew the sample of AAPIs, as English-speaking U.S.-born subjects selectively responded, in which case there would be an underestimation of the prevalence of HBV infection since foreign- born AAPIs would be unlikely to participate.

Our study findings confirm the high prevalence of HBV infection among AAPIs, specifically among AAPIs in regions where AAPIs constitute a small proportion of residents. Given the high incidence of HBV infection among these community-dwelling KA, and that the majority of HBV-infected participants were unaware of their condition, focused HBV screening should be conducted to uncover individuals with HBV. The fact that only 16.7% were aware of their infectious status is of great concern because treatment of chronic HBV is becoming more effective and can prevent or slow the development of liver cancer and cirrhosis.

Conclusions

This study points to the importance of developing multiple strategies for HBV infection prevention. First, it is important to educate health care providers to increase their awareness and knowledge of new CDC guidelines stating that AAPI immigrants and their offspring are high risk for HBV infection and that providers need to increase efforts to detect HBV carriers and vaccinate unprotected AAPIs. Although the diagnosis of HBV infection can be made with a simple blood test, the majority of physicians are unaware of the high incidence of liver cancer and HBV infection among AAPIs. Second, it is important to develop and implement a community-based program that ensures access and incorporates a culturally-sensitive HBV screening and vaccination program rather than waiting for AAPIs to come to traditional clinical settings. This is especially important for immigrants with limited health insurance who are unable to use medical systems in the U.S. Further, this study was carried out in a non-traditional setting and showed that churches are excellent sites for health education and clinical programs for Korean Americans and other AAPIs.

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