ORIGINAL PAPER

Prevalence and Presentation of Hepatitis B and C Virus (HBV and HCV) Infection in Vietnamese Americans via Serial Community Serologic Testing

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Abstract The prevalence of hepatitis B virus (HBV) infection is reportedly high in Vietnamese Americans (VAs), but most previous studies did not assess full HBV serology, and not the prevalence of HBV and hepatitis C virus (HCV) infection simultaneously. The aim of the study is to assess the prevalence of different HBV serologies and HCV infection in VAs. This study was based on the data collected by testing for Hepatitis B surface antigen (HBsAg), anti-hepatitis B core antibody (HBcAb IgG), anti-HBs antibody (HBsAb), and anti-HCV antibody (anti-HCV) in a series of community screening in VAs in Orange County, California. In 1,405 VA participants, the mean age was 51 (17-87) years, 45.1 % were males; 68.2 %, married; 97.2 %, born in Vietnam. Most of the participants were non-US born with their primary language being non-English and with limited access to health care. Of the 1,405 cases, 124 (8.8 %) were confirmed HBV infection by HBsAg+; 81 (5.8 %), HCV infection by anti-HCV+; including four (0.3 %) with HBV/HCV coinfection. Twelve percent of the participants with confirmed

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HBV infection thought they were previously tested negative, while 29.7 % of the participants with confirmed HCV infection thought they were previously tested negative. In this cohort, 15.4 % were HBsAg-/HBsAb-/HBcAb IgG-, i.e. being susceptible to HBV infection. In HCV infected participants, 65.4 % were born between 1945 and 1965. This large serial survey and screening in the Vietnamese American community confirmed the rates of HBV and HCV infection to be as high as 8.8 % and 5.8 %, respectively. We have also identified factors related to HBV and HCV infection in this high-risk population.

Keywords Hepatitis B · Hepatitis C · Vietnamese Americans · Orange County · Prevalence

Abbreviations

AASLD	American association for the study of liver diseases
CDC	Centers for disease control and prevention
HBcAb	Anti-hepatitis B core antibody
IgG	-
HBsAb	Anti-hepatitis B surface antibody
HBsAg	Hepatitis B surface antigen
HBV	Hepatitis B virus
HCC	Hepatocellular carcinoma
HCV	Hepatitis C virus
Anti-HCV	Anti-HCV antibody
VA	Vietnamese American
VACF	Vietnamese American cancer foundation

Introduction

Hepatitis B virus (HBV) infection is one of the major public health issues. Approximately, 350 million people are chronically infected with HBV, accounting for at least half a million deaths per year worldwide [1-3]. Earlier studies estimated 1.4 million Americans being infected by HBV. However, counting on rapidly growing immigrants from high HBV endemic countries/regions, it is estimated that 2.2 million Americans are HBV-infected and 58 % are Asian Americans [4–7]. Chronic hepatitis B may cause cirrhosis and is associated with 200 times higher risk for hepatocellular carcinoma (HCC) compared to non-infected persons [8, 9]. More than 90 % of infected newborns with HBV can become chronically infected, whereas the rate is only 0-10 % with newly infected adults or adolescents [10, 11]. In the United States, the prevalence of HBV infection is speculated to increase, mostly due to immigration from endemic regions [4]. In fact, chronic HBV infection in the Asian-American population has gained a lot of attention as it is responsible for 80 % of HCC in this specific population [12, 13]. The American association for the study of liver diseases (AASLD) has suggested routine screening for chronic HBV infection and HCC among people of this population [14–17].

On the other hand, chronic hepatitis C virus (HCV) infection has affected 170 million people worldwide and causes 280,000 deaths per year [18, 19]. In the United States, it is estimated that there are 3.9 million chronically HCV infected people [18, 20]. In the Asian American community, the prevalence of chronic HCV infection was reported low by small cohort studies [21], but the real prevalence remains to be determined.

Among Asian subgroups in the United States, Vietnamese Americans (VAs) are the second fastest growing Asian group (just behind Filipino Americans) with a population of over 1.25 million [22, 23] and is projected to reach 4 million in 2030 [24]. Previous data have shown that the prevalence of chronic HBV infection was 7-14 % among VAs [25-28] in comparison to 8-10 % of the Vietnamese population in Vietnam, which is equivalent to about 7 million chronic HBV infection carriers [29]. What strikes the most about this community is that VA males are subject to HCC more than any other ethnic groups [25] and the major etiology of these HCC cases is chronic HBV infection [12, 30, 31]. One of the latest studies by Kallman et al. reported that in 322 tested VAs in Northern Virginia, 9.3 % were positive for HBsAg and 2.2 %, positive for anti-HCV, respectively [32]. However, other HBV serologic tests, such as HBsAb and HBcAb IgG, were not included in this study. There have been no such studies in Southern California, the region where most VAs live in.

Orange County in California is the third most populated county by Asians in the country and has the highest concentration of VAs out of all counties across the nation [33]. Vietnamese American Cancer Foundation (VACF) has conducted a series of HBV and HCV screening in this community, including a detailed survey and serologic tests comprising of HBsAg, HBsAb, HBcAb IgG, and anti-HCV that allowed us to assess not only the prevalence of HBV and/or HCV infection but also HBV susceptibility, HBV immunity, and past HBV infection in VAs.

Patients and Methods

Patient Population

This study was based on a series of hepatitis B and C screening in VA community in Orange County, California conducted by VACF between August 2008 and August 2010. The screening took place in the setting of biannual health fairs conducted by VACF. Consents for blood draw and participating in the study were obtained from each participant. A total of 1,405 consecutive individuals participated in the screening.

Methods and Data Collection

Specific serologic tests for the screening include HBsAg, HBcAb IgG, HBsAb, and anti-HCV. In addition to these laboratory tests, a questionnaire was issued to all participants. The survey was designed to collect demographic and clinical data such as age, year of birth, gender, primary speaking language, marital status, country of birth, mother's country of birth, father's country of birth, years of residency in the US, highest education, family member with hepatitis B, number of household members, household member(s) with hepatitis B, history of being told to have hepatitis B, history of being medicated for either hepatitis B or C, history of hepatitis B vaccination, history of seeking treatment 6 months since diagnosis, number of participation in the screening, medical insurance status, and whether to have a healthcare provider. If a patient was tested positive for either HBV or HCV, he or she would be notified via contact information provided at the time of blood collection. Nine individuals participated in the screening twice while no one participated three or four times. The duplicates were excluded from data analysis.

Statistical Analysis

The descriptive data were shown as whole numbers and percentages. Chi square tests were performed in comparison among variables to assess associations between independent factors with HBV and HCV infections. A p value of <0.05 is considered statistically significant.

 Table 1
 Baseline demographics and clinical characteristics of the survey participants

Variables	Total cases	Reported cases	Percentage
Age ≥ 50	1,403	843	60.1
Male gender	1,405	634	45.1
Married	1,379	941	68.2
Non-english speaking	1,382	1,268	91.8
Born in Vietnam	1,401	1,373	97.2
Years in residency			
<10 years	1,377	357	25.9
10-20 years	1,377	542	39.4
>20 years	1,377	478	34.7
Annual income			
0–20 K	931	595	63.9
20–40 K	931	231	24.8
>40 K	931	105	11.3
Highest education			
≤High school	1,398	856	61.2
≥College	1,398	542	38.8
With health insurance	1,399	723	51.7
With a primary care provider	1,379	722	52.4
Able to afford HBV treatment	1,396	630	45.1

Results

Baseline Demographics

In 1,405 VA participants, 45.1 % were male; 843/1,403 (60.1 %) participants were 50 year-old or older; 941 of 1,379 (68.2 %), married; 1,268/1,382 (91.8 %) reported that their primary language was not English; and 595/931 (63.9 %) had annual income lower than 20,000 US dollars. Of 1,403 participants, 160 (11.4 %) were born before 1945, 859 (61.2 %) were born between 1945 and 1965, and 384 (27.4 %) were born after 1965. Of 1,401 individuals reported, 1,373 (98 %) were born in Vietnam; 856/1,398 (61.2 %) individuals had highest education as high school or less. As shown in Table 1, 723/1,399 (51.7 %) participants had health insurance; 722/1,379 (52.4 %) participants had a healthcare provider.

Prevalence of HBV and HCV Infection

As summarized in Table 2, 124/1,405 (8.8 %) participants were tested positive for HBsAg, consistent with HBV infection; and 81/1,405 (5.8 %) participants were tested positive for anti-HCV. Four individuals (0.3 %) were tested positive for both HBsAg and anti-HCV. Of 81 HCV infected participants, 53 (65.4 %) were born between 1945 and 1965.

Markers	Cases (N = 1,405)	Percentage
HBsAg+	124	8.8
HCVAb+	81	5.8
HBsAg+/HCVAb+	4	0.3

Table 3 HBV Infection Status (N = 1,405)

Serologic findings	Interpretation	Cases	Percentage
HBsAg–/HBsAb–/ HBcAb IgG–	Susceptible to HBV	217	15.4
HBsAg-/HBsAb+/ HBcAb IgG-	Immune to HBV	308	21.9
HBsAg-/HBsAb+/ HBcAb IgG+	Past HBV infection	624	44.4
HBsAg-/HBsAb-/ HBcAb IgG+	Isolated HBcAb IgG positive	132	9.4
HBsAg+/HBsAb-/ HBcAb IgG+	On-going HBV infection	118	8.4
HBsAg+/HBsAb+/ HBcAb IgG+	On-going HBV infection	6	0.4

A major difference of the present study with previous reports is that the detailed HBV serologic tests, including HBsAg, HBcAb IgG, and HBsAb, were performed, which allowed us to assess not only prevalence of ongoing HBV infection, but also past HBV infection and immunity or susceptibility to HBV infection. Table 3 provides a detailed summary on different HBV serologic results. A total of 124 (8.8 %) participants were considered as HBVinfected by positive HBsAg. Of these 124 infected individuals, 118 (8.4 %) subjects were HBsAg+/HBsAb-/ HBcAb IgG+ and six (0.4 %) individuals were HBsAg+/ HBsAb+/HBcAb IgG+. On the other hand, 217 (15.4 %) participants were tested negative for HBsAg, HBsAb, and HBcAb IgG, i.e., being susceptible to HBV infection and in need of HBV vaccination; 308 (21.9 %) participants were HBsAg-/HBsAb+/HBcAb IgG-, i.e., HBV immune via vaccination; and 624 (44.4 %) participants were tested HBsAg-/HBsAb+/HBcAb IgG+, i.e., being exposed to HBV in the past with current immunity against HBV. A small proportion of participants (132/1,405, 9.4 %) was tested HBsAg-/HBsAb-/HBcAb IgG+, a situation that could be secondary to past HBV infection with loss of immunity against HBV or false positive testing.

Factors Related to HBV Infection

As summarized in Table 4, certain factors are statistically different among HBV susceptible patients, HBV immune patients, patients with past HBV infection or isolated HBcAb IgG+, and patients with active HBV infection.

Variables	Cases	Susceptible to HBV	Immune to HBV	Past HBV infection or isolated HBcAb+	HBV infection	P value
Age \geq 50	1,322	98/206 (47.6 %)	133/297 (44.8 %)	494/699 (70.7 %)	61/120 (50.8 %)	< 0.001
Gender (male)	1,324	78/207 (37.7 %)	119/297 (40.1 %)	333/700 (47.6 %)	64/120 (53.3 %)	0.005
Marital status (married)	1,301	121/203 (59.6 %)	163/289 (56.4 %)	514/690 (74.5 %)	80/119 (67.2 %)	< 0.001
Living with someone who has hepatitis B	1,316	12/205 (5.8 %)	28/293 (9.6 %)	64/698 (9.2 %)	23/120 (19.2 %)	0.004
Was told to have hepatitis B	1,305	41/205 (20.0 %)	108/290 (37.2 %)	221/692 (31.9 %)	68/118 (57.6 %)	< 0.001
Previously medicated for hepatitis B or C	1,303	5/205 (2.4 %)	4/292 (1.4 %)	12/687 (1.8 %)	18/119 (15.1 %)	< 0.001
Hepatitis B vaccination	1,306	38/205 (18.5 %)	110/292 (37.7 %)	111/690 (16.1 %)	14/119 (11.8 %)	< 0.001
Having health insurance	1,319	103/207 (49.8 %)	157/295 (53.2 %)	375/696 (53.8 %)	49/120 (40.8 %)	0.06
Having a primary care provider	1,299	96/202 (47.5 %)	159/290 (54.8 %)	383/688 (55.7 %)	45/119 (37.8 %)	0.001

Table 4 Characterization of the different status in HBV infection

These variables are age ≥ 50 years (p < 0.001), male gender (p = 0.005), being married (p < 0.001), living with someone who has hepatitis B (p = 0.004), being told to have HBV infection (p < 0.001), previously medicated for hepatitis B or C (p < 0.001), history of HBV vaccination (p < 0.001), and having a primary care provider (p = 0.001). The past HBV infection/isolated HBcAb IgG positivity group has the highest proportion of individuals that are ≥ 50 years old (70.7 %). This group of patients is also found to have more married patients (74.5 %) than any other groups. In the group with active HBV infection, 19.2 % live with someone who had hepatitis B, which is the highest among the groups. This group also leads in the number of patients being previously medicated for either hepatitis B or C (15.1 %) or being told to have hepatitis B (57.6 %). Although there is no statistically significant difference between the four groups in terms of having a health insurance plan (p = 0.06), the active HBV infection group is found to have the significantly least patients with a primary care provider (37.8 %, p = 0.001) compared to the HBV susceptible group (47.5 %), the immune to HBV group (54.8 %), and the past HBV infection/isolated HBcAb IgG+ group (55.7 %).

Comparison of the Participants with HBV versus HCV Infection

Table 5 summarized differences in demographics and characteristics between hepatitis B patients and hepatitis C patients in the study. A significantly higher percentage of patients with HCV infection (70.1 %) was found to be \geq 50 years old, compared to 50.8 % in HBV infection group (p = 0.007). A significantly higher proportion of HBV-infected individuals (39.0 %) had an annual earning \leq 10,000 dollars, compared to the HCV-infected individuals (24.1 %, p = 0.047). Twenty percent of the HBV-infected individuals thought they were previously tested negative for hepatitis B, in contrast to 29.7 % of the

HCV-infected individuals (p = 0.004). Participants who had been tested or told about their disease status, but did not know or remember then accounted for 12.1 % and 27.0 % of the HBV or HCV-infected individuals, respectively. Although there is no statistical difference, it is worth mentioning that 45.8 % of the HBV-infected individuals sought treatment 6 months since diagnosis, compared to 39.0 % in the HCV-infected individuals.

Discussion

The prevalence of HBV and HCV infection has not been thoroughly studied in different Asian ethnicities in the United States. Many studies on HBV or HCV infection in VAs were survey or cross sectional studies that lacked either detailed characterization of the diseases or statistical power due to relatively small sample size. In this study, we not only were able to serologically assess HBV and HCV infection prevalence, but also determined the status of HBV infection by differentiating between HBV susceptible, HBV immune, and HBV infected individuals in a large cohort of VAs living in Orange County, California. This provided us a unique opportunity to reliably assess these issues in a special Asian subgroup that is usually underrepresented.

In our study, we demonstrated that the prevalence of HBV infection, defined as being positive for HBsAg, was 8.8 % in VAs. This finding is comparable with other reports about HBV infection rate in the Vietnamese American community, which was estimated between 7.0 % and 14.0 % [25–28, 32, 34]. In general, the prevalence of HBV infection is known to be much higher among Asian Americans compared to other ethnicities. Half of 1.3 million chronic HBV carriers in the United States are Asian Americans. The prevalence of HBV infection among non-Hispanic whites in the US is about 1.0 % compared to 10.0 % in the Asian American population [35, 36].

Table 5 Fact	ors associated	with HBV	versus HCV	infection
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Variables	Total cases	Factors related to HBV infection	Factors related to HCV infection	p value
Age ≥50	197	61/120 (50.8 %)	54/77 (70.1 %)	0.007
Gender (male)	197	64/120 (53.3 %)	37/77 (48.1 %)	0.5
Income	136			
<10 K		32/82 (39.0 %)	13/54 (24.1 %)	0.047
10–50 K		43/82 (52.5 %)	41/54 (75.9 %)	
>50 K		7/82 (8.5 %)	0/54 (0.0 %)	
Family members with hepatitis B	196	44/119 (37.0 %)	14/77 (18.2 %)	<0.001
Family members with hepatitis C	34	2/19 (10.5 %)	0/15 (0.0 %)	0.1
Living with someone with hepatitis B	196	23/120 (19.2 %)	4/76 (5.3 %)	0.02
Ever been tested or told to have hepatitis	194	68/118 (57.6 %)	38/76 (50.0 %)	0.5
If, yes what was the result?	103			
Positive		50/66 (75.8 %)	16/37 (43.3 %)	0.004
Negative		8/66 (12.1 %)	11/37 (29.7 %)	
Don't know		8/66 (12.1 %)	10/37 (27.0 %)	
History of being medicated for either hepatitis B or C	194	18/119 (15.1 %)	9/75 (12.0 %)	0.7
Being vaccinated for hepatitis B	196	14/119 (11.8 %)	18/77 (23.4 %)	0.08
Seeking treatment after 6 months	197	55/120 (45.8 %)	30/77 (39.0 %)	0.3

Besides the prevalence of HBV infection, knowing other HBV statuses, such as immunity and susceptibility to HBV, will be important for future strategy to further reduce prevalence of HBV infection. In the present study, 15.4 % of the participants were found to be susceptible to HBV infection, evidenced by HBsAg-/HBsAb-/HBcAb IgG-. Of note, 49.8 % of those who are susceptible to HBV and need hepatitis B vaccination have health insurance. Therefore, this finding indicated that further efforts should be exercised to improve access to HBV vaccination in this subgroup, which is still at risk for HBV infection.

In this cohort of participants, 21.9 % were confirmed as being immune to HBV infection, which was evidenced by HBsAg-/HBsAb+/HBcAb IgG-. These participants had a younger mean age, a possible reason to have received HBV vaccinations. It should also be noted that 14/124 (11.3 %) HBV infected participants reported "received HBV vaccination", but their serology confirmed HBV infection. This indicates needs to educate primary care providers to screen for HBV infection prior to administration of HBV vaccination.

We also found that 44.4 % of all screened participants were exposed to HBV in the past and are now immune to HBV, confirmed by the serology of HBsAg-/HBsAb+/HBcAb IgG+. This group of participants had significantly higher mean age, consistent with spontaneous HBV clearance after a long history of chronic HBV infection, as previously reported [37]. Given the fact that 97.2 % of participants were born in Vietnam, it is not surprising about this high rate of past HBV infection in these VA participants.

In literature, the concurrence of HBsAg and HBsAb positivity is observed in 23.9–32.0 % of HBsAg+ patients [38–40]. In our cohort of participants, 6/124 (4.8 %) with chronic HBV infection were tested positive for both HBsAg and HBsAb. The presence of both HBsAg and HBsAb in these individuals may suggest HBsAb is unable to neutralize circulating virions, making these individuals HBV carriers. This phenomenon is more common in chronic hepatitis B than acute hepatitis B [38, 39].

Serology can differentiate four statuses related to HBV infection, namely HBV susceptible, HBV immune, previously HBV infected, and actively HBV infected. In the univariate analysis, we noticed there were significant characteristic differences between the four HBV infection statuses in terms of age, gender, marriage status, living with someone who has hepatitis B, being told to have HBV infection, previously medicated for hepaitits B or C, history of HBV vaccination, and having a primary care provider. However, a multi-variate analysis for all four stages of HBV infection with all the mentioned factors was not feasible. When comparing the participants with different HBV statuses, the active HBV infection group leads as regards to the number of participants currently living with someone with hepatitis B (19.2 %). More importantly, 12.1 % of these participants with active HBV infection believed they were not infected with HBV and another 12.1 % did not know about their disease status. Our findings of a combined number of 24.2 % of patients who were unclear about their HBV infection status emphasizes the importance in disease awareness and other preventive measures for hepatitis B in the Vietnamese American

community. Knowing one's disease status as well as other family members' disease status potentially helps reduce disease transmission among family members in specific, or horizontal transmission in general.

Moreover, only 45.8 % of HBV infected participants actively sought for HBV-related care 6 months after being diagnosed. This finding underlines the importance of making hepatitis B treatment available for this high risk population in addition to close follow-ups and patient education.

HCV infection is not well-emphasized in Asian Americans in general and VAs in specific. In our large cohort of 1,405 VAs who received the screening, the prevalence of HCV infection was found to be 5.8 %. This number is higher than previously reported rate of 2.2 % in VAs in Virginia [32]. More importantly, HCV infection rate of 5.8 % in the VAs confirmed by the present study is much higher than the 1.8 % HCV prevalence previously reported in this country [18, 20, 41].

According to centers for disease control and prevention (CDC), three-fourths of chronic HCV infected people in the United States were born between 1945 and 1965 and the prevalence of HCV infection in this specific population is 3.25 % [50, 51]. Hence, CDC updated its recommendations that all people that were born during this period should be screened for HCV infection despite their risk profiles [50]. In our cohort, 65.4 % of anti-HCV+ were born between 1945 and 1965, consistent with CDC data. Therefore, the updated CDC recommendations for HCV screening among the people born between 1945 and 1965 also apply to the VA population.

A large number of HCV infected patients have poor health care access [50, 52]. In our cohort, more than 50.0 % of HCV-infected participants have no insurance or health care providers (51.3 % and 51.3 %, respectively). Only 39.0 % actively sought HCV-related care 6 months since being diagnosed with HCV infection. Thus, our future efforts should focus on providing this special population with access to HCV-related care.

In our study, we also found the baseline demographics are different between HBV-infected and HCV-infected participants. A higher percentage of patients of 50+ years of age was found in HCV-infected individuals when compared to HBV-infected individuals (p = 0.007). HCVinfected participants had a significantly lower positive family history or living with an infected family member. These may be related to the differences in mode of transmission and age of HCV infection versus HBV infection [42–44].

Worldwide, the prevalence of HBV/HCV co-infection is unknown due to lack of large-scale population-based studies. Generally speaking, 2-10 % of anti-HCV+ patients are found to be HBsAg+ whereas 5-20 % of chronic hepatitis B patients are found to be anti-HCV+ [45]. In our study, almost half of HCV infected participants have past HBV infection; yet, only 4/81 (4.9 %) HCV infected participants were confirmed as HBV/HCV co-infected. The low prevalence of HBV and HCV co-infection is probably due to viral interference, also called reciprocal replicative suppression of the two viruses, a phenomenon that is still under ongoing evaluation [46– 48]. However, to be able to accurately estimate the prevalence of HBV/HCV co-infection among VAs, we might need a much larger sample size.

Shortcomings do exist in our study. Our study did not have a full spectrum of the related tests, such as HBeAg, anti-HBe, HBV DNA, HCV RNA, AST, and ALT to evaluate viral replication, viral infectivity, and severity of liver disease [49]. The number of questions issued to the participants were carefully chosen and limited as we could not provide the health fair participants with a long list of questions, provided that most people who go to a health fair would find that a turn-off to participate in a survey. In addition, this study did not collect data on participants' occupations, which is useful in demographic stratification. Furthermore, our database is partially compromised by recall bias as the survey questionnaires required the participants to recall about their personal history related to HBV and HCV infections.

In conclusion, the prevalence of HBV and HCV infection via serologic testing among VAs are 8.8 % and 5.8 %, respectively. HCV infected participants born between 1945 and 1965 accounted 65.4 % of all HCV infected participants, which supports CDC data and its new guideline in screening all people that were born between 1945 and 1965 for hepatitis C. A large proportion of the participants were not aware of their disease status, either HBV or HCV infection; hence, aggressive routine screening and educating VAs for both hepatitis B and C in this Asian American subgroup is highly recommended.

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