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Hepatitis B Virus Infection Testing and Prevalence Among Asian and Pacific Islanders

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Abstract

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Objectives: Asian and Pacific Islanders (APIs) constitute less than 6% of the US population, but account for more than half of Americans with chronic hepatitis B virus (HBV) infection. We sought to examine the effect of country of origin on HBV testing and chronic HBV infection prevalence among APIs.

Methods: We analyzed demographic and clinical data collected for adults from Kaiser Permanente Hawaii with 1 or more healthcare encounters during 2006 to 2008, 12 months or more of follow-up before 2009, and no HBV-related diagnosis within 6 months of enrollment. Persons who received a test and a positive test result for HBV surface antigen or HBV DNA were classified “tested” and with “chronic HBV infection”, respectively.

Results: Of 92,687 eligible APIs, 53,573 (58%) had country-of-origin data available. Among those, 41,263 were US born; 28.3% were tested; and 1.8% of those tested had chronic HBV infection. Of 12,310 foreign-born APIs, 30.5% were tested and 7.4% of those tested had chronic HBV infection. Foreign-born APIs had higher odds of being tested (odds ratio [OR] = 1.15) and testing positive (OR = 4.18) compared with US-born APIs. Persons with 2 or more abnormal tests for alanine aminotransferase (ALT) levels had higher odds of getting tested (OR = 6.12) and of testing positive (OR = 1.86) compared with persons with other ALT levels.

Conclusions: Less than one-third of this managed care API population (29% of 53,573) was tested, yet the prevalence of chronic HBV infection (3.2%) was 12 times higher than that of the general US population. These findings underscore the importance of adherence to HBV testing guidelines to identify persons with infection so they may be linked to care.

In the United States, between 800,000 and 2 million people live with chronic hepatitis B virus (HBV) infection and 2000 to 4000 deaths are attributed to HBV infection annually.¹⁻⁴ Cirrhosis and hepatocellular carcinoma (HCC) are 2 major long-term complications of chronic HBV infection that significantly increase morbidity and mortality. Asian and Pacific Islanders (APIs) make up less than 6% of the US population but account for more than half of Americans living with chronic HBV infection^{5,6}; hepatocellular carcinoma (HCC) rates are highest among APIs, and HCC is a leading cause of cancer deaths in this population.⁷⁻⁹ Most APIs with chronic HBV infection acquire their infection at birth through mother-to-child transmission or during childhood.¹⁰

In 2009, an estimated 1.32 million foreign-born individuals with chronic HBV infection were thought to be living in the United States, and 58% of those persons migrated from Asia, where HBV infection is highly endemic.² The population makeup of Hawaii, the 50th US state, includes 47% persons of Asian descent and 29% persons of Native Hawaiian/Pacific Islander descent.^{5,11,12} Among Hawaii’s 212,229 foreign-born residents in 2000, 73% were born in countries with endemic HBV infection, including China, Vietnam, the Philippines, and elsewhere among the South Pacific Islands.¹³

In Hawaii, Kaiser Permanente (KPHI) has approximately 220,000 members and is the largest health maintenance organization (HMO) providing care in the state.¹⁴ Commensurate with the high representation of APIs living in Hawaii, APIs constitute approximately half of KPHI’s membership. Given the unique demographic conditions in Hawaii relative to other US states, and our access to demographic and clinical data collected from patient

encounters, we sought to examine the effect of country of origin on HBV infection testing and prevalence among APIs at KPHI.

METHODS

Persons eligible for the study included those who: (1) were aged 18 years or older; (2) had at least 1 KPHI clinical encounter at any time during January 1, 2006, to December 31, 2008; and (3) completed at least 12 months of continuous follow-up any time before 2009. To examine HBV infection testing and prevalence among persons without previously diagnosed infection, we excluded those with any HBV-related *International Classification of Diseases, Ninth Revision (ICD-9)* diagnosis code within 6 months of their first KPHI clinical encounter. Retrospective electronic data were available through January 1, 1998.

Patient data were collected from electronic medical records and included age (as of last encounter before December 31, 2008), gender, race/ethnicity, annual income (derived from census tract data based on geocode), and serum alanine aminotransferase (ALT) level. Abnormal ALT was defined as a level higher than the lab-specific upper limit of normal value (range: 3-63 IU/L). Data were collected from the date of the patient's earliest health plan enrollment through the last health plan encounter, ending December 31, 2008. Methods were identical to those used in an earlier analysis of hepatitis testing and prevalence among 1.2 million persons in 4 healthcare organizations including KPHI, but which lacked country-of-origin data.¹⁵ Briefly, persons were classified as "tested" if they had at least 1 test performed for HBV surface antigen (HBsAg) or a qualitative or quantitative test for HBV DNA; those classified with "HBV infection" had at least 1 positive result for any of these tests. The number of persons with infection divided by the number of persons tested was calculated to determine HBV infection prevalence. APIs were classified as foreign born (birth in Asian or Pacific Island countries) or US born (birth in the United States or Canada), based on the self-reported country of origin.

This study was reviewed and approved by the KPHI Institutional Review Board and followed guidelines of the US Department of Health and Human Services for protection of human subjects.

Statistical analysis was performed using SAS, version 9.2 (SAS Institute Inc, Cary, North Carolina). Chi-squared test (χ^2) was used to ascertain differences in characteristics between US-born and foreign-born APIs.

RESULTS

Study Population

After exclusion of 198 persons with an HBV-related *ICD-9* diagnosis code within 6 months of their first KPHI clinical encounter, a total of 189,550 KPHI adults met the study inclusion criteria. Among eligible adults, 92,687 (48.9%) were APIs. Information on country of origin was available for 53,573 persons: 12,310 (23%) were born in Asian and Pacific Island countries and 41,263 (77%) were born in the United States (n = 41,235) or Canada (n = 28).

Among all APIs (N = 53,575), 29% (n = 15,439) were tested for HBV infection and, among those tested, 3.2% (n = 494) were infected.

The principal demographic and clinical characteristics of the US and foreign-born APIs are presented in Table 1. Compared with foreign-born APIs, US-born APIs were more likely to be younger than age 30 years or older than age 69 years. Foreign-born APIs were more likely to be female, to have lower annual incomes, and to have had at least 2 abnormal ALT test results before undergoing HBV infection testing. A greater proportion of foreign-born APIs were tested and a greater proportion had HBV infection compared with US-born APIs (tested: 3752 [30.5%] vs 11,687 [28.3%]; tested positive: 279 [7.4%] vs 215 [1.8%]). Among APIs with at least 2 abnormal ALT test results, 46% of foreign-born and 41% of US-born were tested for HBV infection, 8.6% of foreign born and 1.9% of US-born were infected.

Table 2 show the important factors associated with odds of getting tested and testing positive for HBV infection. Individuals aged 30 to 39 years had higher odds of getting tested and of testing positive than other age groups. Females had higher odds of getting tested than males. Repeating the analysis excluding the pregnant women who were ever tested for HBsAg (n = 7092), the odds ratio (OR) for females attenuated from 3.26 to 1.13 (data not shown). Foreign-born APIs had higher odds of being tested (OR = 1.15) and testing positive (OR = 4.18) compared with US-born APIs. Persons with at least 2 or more abnormal ALT tests had higher odds of getting tested (OR = 6.12) and testing positive (OR = 1.86) compared with other ALT levels. Repeating the analysis with pregnant women excluding OR for foreign-born APIs and ALT levels did not produce results that differed much.

Table 3 shows the proportion of foreign-born APIs who were tested and infected with HBV by country of birth. Among the 12,310 foreign-born APIs, 11,058 (89.8%) were from countries with high HBV endemicity (ie, HBsAg prevalence 8%)¹⁶; of these, 29.9% were tested for HBV infection and 7.9% of those were positive for HBV infection. The remaining 10.2% of foreign-born APIs were from countries with intermediate HBV endemicity (ie, HBsAg prevalence 2%–7%)¹⁵; of these, 29.8% were tested and 2.7% were positive for HBV infection. Among all foreign-born APIs tested, the proportion of those infected ranged from 2.7% (Japan) to 12.3% (China). Approximately 50% of the foreign-born APIs were from the Philippines; of these, 29.9% were tested and 5.5% were positive for HBV infection.

DISCUSSION

In this study of HBV testing and infection prevalence among APIs in a large HMO, we found that less than one-third of persons without a HBV diagnosis code at enrollment were tested for HBV infection. Among APIs who were tested, the prevalence of HBV infection (3.2%) was almost 12 times higher than that of the general US population (HB-sAg prevalence 0.27%). Among foreign-born APIs who were tested, 90% of whom were born in countries with high HBV endemicity, infection prevalence was largely commensurate with that of their country of origin (7.5% overall). These findings support US Centers for Disease Control and Prevention (CDC) guidelines that recommend HBV infection screening for

pregnant women, persons with high-risk behavior, and those born in Asia, Africa, and other geographic areas where HBsAg prevalence exceeds 2%.³

Even among US-born APIs, the prevalence of HBV infection was high (1.8%) relative to the general US population. Maternal country of birth information among US-born APIs might have permitted differentiation of first generation “API Americans” from those whose families had resided in the United States for multiple generations, and may have permitted further differentiation of infection prevalence; however, we did not have access to such information.

Results were compared with those from other studies. For example, a study by Lin et al reported HBV prevalence to be almost double (6.2%, 185 of 2973) that found in our study among previously undiagnosed API adults, and foreign-born APIs (10.7% HBsAg-positive test result) were approximately 20 times more likely to be chronically infected than US-born APIs (0.7% HBsAg-positive test result; RR 19.4, 95% CI, 2.6-141.8.¹⁷ Two other US-based studies—1 conducted in Hawaii (overall HBsAg prevalence, 3.6%)¹³ and another that used university students in California as study subjects (overall HBsAg prevalence of 2.3%, 1.4% in US-born and 3.3% in foreign-born APIs)¹⁸— assessed HBV infection prevalence, and results of those studies more closely aligned with our results, although these studies did not limit their analysis to APIs and had an age range of 18 to 21 years. In our study, perhaps most remarkable was that among APIs with a history of at least 2 abnormal ALT tests, fewer than 50% were tested for HBV infection. CDC and the American Association for the Study of Liver Diseases guidelines recommend testing persons with unexplained abnormal liver enzyme tests for HBV (and hepatitis C virus) infection.¹⁹

Our study had a number of limitations. In order to ensure assessment of persons with sustained followup, eligibility criteria for the study required at least 12 months of continuous follow-up any time before 2009. We acknowledge that some persons could have been tested in 2009 or thereafter and not included in our analysis. In addition, although we excluded those with an HBV *ICD-9* diagnosis code within 6 months of their first clinical encounter, some persons could have previously tested negative for HBV infection or been vaccinated for HBV in another healthcare setting prior to our period of study, and might not need to be tested again. Secondly, from a case definition standpoint, we used a single HBsAg or HBV DNA to define testing for and infection with HBV. Although most of these infections were chronic, it is conceivable that some were actually acute. Given the low incidence of acute HBV infection in the United States, however, it is unlikely that such misclassification would have appreciably affected our results.

Finally, we recognize that the estimates of testing frequency and infection prevalence in our cohort are not necessarily reflective of all private and public healthcare systems in the United States. Nonetheless, our study had a large sample size and was conducted in a setting with high representation of persons of API descent.

CONCLUSIONS

In summary, we found that less than one-third of this API population in managed care were tested for HBV infection and that among those tested, the prevalence of HBV infection was nearly 12 times higher than that of the overall US population. Infection prevalence among foreign-born APIs was similar to that of their country of origin. The prevalence of HBV infection among US-born APIs was almost 7 times higher than for the overall US population. These findings underscore the importance of adherence to current US guidelines that recommend HBV testing of persons born in countries with intermediate and high HBV endemicity, and the testing of US-born persons whose parents were born in such countries. At KPHI, country-of-birth information is not collected routinely. The results of this paper might provide evidence of the importance of collecting such information routinely in our health system. Sensitivity analysis has shown the cost-effectiveness of HBV screening, even with the prevalence of chronic HBV infection as low as 1%,²⁰ and hence it is important to focus HBV screening efforts on high-prevalence groups such as foreign-born APIs. Persons found to be susceptible to infection should be vaccinated, and those found to have infection should be evaluated for treatment.

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Take-Away Points

Hepatitis B virus (HBV) infection prevalence among foreign-born Asian and Pacific Islanders (APIs) living in the United States was similar to that found in their country of origin. The prevalence of HBV infection among US-born APIs was almost 7 times higher than it was for the overall US population. These findings underscore the importance of adherence to current US guidelines that recommend HBV testing of persons born in countries with intermediate and high HBV endemicity, and the testing of US-born persons whose parents were born in such countries. Persons found to be susceptible to infection should be vaccinated, and those found to have infection should be evaluated for treatment.

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Table 1. Demographic Differences Between Foreign-Born and US-Born Asian and Pacific Islanders (APIs)

Characteristics	Foreign-born APIs	US-born APIs	P
Total	12,310	41,263	
Mean age (years ± SD)	50.5 ± 15.7	50.0 ± 19.5	.003 ^a
Age groups (10 y)			
<30	1213 (9.9%)	7806 (18.9%)	<.001 ^b
30-39	2016 (16.4%)	6220 (15.1%)	
40-49	2628 (21.4%)	6497 (15.8%)	
50-59	2938 (23.9%)	7235 (17.5%)	
60-69	2016 (16.4%)	5897 (14.3%)	
70-79	1027 (8.3%)	4227 (10.2%)	
80	472 (3.8%)	3381 (8.2%)	
Female	7444 (60.5%)	22,908 (55.5%)	<.001 ^b
Annual income^c			
<\$30K	1001 (8.3%)	2144 (5.3%)	<.001 ^b
\$30K-\$49K	4202 (34.6%)	12,718 (31.2%)	
\$50K-\$74K	5717 (47.1%)	20,396 (50.0%)	
\$75 K	1219 (10.0%)	5571 (13.6%)	
ALT level before testing			
No abnormal ALT level tests	10,903 (88.6%)	36,314 (88.0%)	.015 ^b
1 abnormal ALT level test	73 (0.6%)	186 (0.5%)	
2 abnormal ALT level tests	1334 (10.8%)	4763 (11.5%)	
Tested for HBV infection	3752 (30.5%)	11,687 (28.3%)	<.001 ^b
Positive test result for HBV infection	279 (7.4%)	215 (1.8%)	<.001 ^b

ALT indicates alanine transaminase; HBV, hepatitis B virus; SD, standard deviation.

^a *t* test.

^b χ^2 .

Based on Census tract geocode and missing values for 605 records.

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Factors Associated With Testing and a Positive Test Result for Hepatitis B Virus Infection Among Asian-Pacific Islanders (APIs) Adjusted for Length of Enrollment (N = 53,573)

Table 2.

Characteristics	n	Tested n (%)	Multivariate Adjusted OR (95% CI)	Positive Test Result n (%)	Multivariate Adjusted OR (95% CI)
Age group (years)			Ref	60 (1)	Ref
<30	9019	3250 (36.0)			
30-39	8236	3814 (46.3)	1.36 (1.27-1.45)	108 (1.3)	1.43 (1.04-1.97)
40-49	9125	2569 (28.2)	0.50 (0.47-0.53)	101 (1.1)	1.03 (0.74-1.43)
50-59	10,173	2267 (22.3)	0.31 (0.29-0.34)	123 (1.2)	1.05 (0.76-1.46)
60-69	7913	1749 (22.1)	0.30 (0.28-0.32)	70 (1)	0.80 (0.56-1.15)
70-79	5254	1122 (21.4)	0.28 (0.25-0.30)	24 (0.5)	0.45 (0.28-0.73)
80	3853	668 (17.3)	0.20 (0.18-0.22)	8 (0.2)	0.24 (0.12-0.51)
Gender			Ref	203 (0.9)	Ref
Male	23,221	4141 (17.8)			
Female	30,352	11,298 (37.2)	3.26 (3.12-3.41)	291 (1.0)	1.04 (0.87-1.25)
Annual income^a			Ref	49 (1.6)	Ref
<\$30K	3145	896 (28.5)			
\$30K-\$49K	16,920	4939 (29.2)	0.96 (0.88-1.04)	181 (1.1)	0.79 (0.58-1.07)
\$50K-\$74K	26,113	7532 (29.8)	0.95 (0.88-1.03)	213 (0.8)	0.63 (0.46-0.85)
\$75K	6790	1861 (27.4)	0.97 (0.88-1.07)	45 (0.7)	0.57 (0.38-0.85)
Country of origin			Ref	215 (0.5)	Ref
US-born APIs	41,263	11,687 (28.3)			
Foreign-born APIs	12,310	3752 (30.5)	1.15 (1.1-1.21)	279 (2.3)	4.18 (3.48-5.02)
ALT level			Ref	402 (0.9)	Ref
No abnormal test	47,217	12,055 (25.5)			
1 abnormal test	259	26 (10.0)	0.78 (0.57-1.07)	1 ^b (3.9)	0.37 (0.05-2.63)
2 abnormal tests	6097	2586 (42.4)	6.12 (5.76-6.51)	91 ^b (3.5)	1.86 (1.47-2.35)

ALT indicates alanine transaminase; CI, confidence interval; OR, odds ratio.

^aBased on Census tract geocode and missing 605.

^bTested positive after 1 (n = 26) or 2 (n = 2586) abnormal ALT levels.

Boldfaced cells indicate increased odds ratios that are significant.

Table 3. Rates of Being Tested and Testing Positive for Hepatitis B Virus Infection by Country of Origin Among Foreign-Born Asian-Pacific Islander Enrollees (n = 12,310)

Country of Birth	TotalN	Tested n (%)	Positive n (%)
All foreign-born	12,310	3752 (30.5)	279 (7.4)
Intermediate-prevalence countries	1252	370 (29.6)	10 (2.7)
Japan	1161	333 (28.7)	9 (2.7)
Others ^a	91	37 (40.7)	1 (2.7)
High-prevalence countries	11,058	3382 (30.6)	269 (79)
Philippines	6136	1784 (29.0)	99 (5.5)
China	708	244 (34.5)	30 (12.3)
Others ^b	4214	1354 (32.1)	140 (10.3)

Intermediate prevalence indicates hepatitis B surface antigen prevalence of 2% to 7%; high prevalence, hepatitis B surface antigen prevalence 8%.

^a,"Others" includes: India (N = 66); Pakistan (N = 13); Bangladesh (N = 6); Nepal (N = 6).

^b,"Others" includes: South Korea (N = 688); American Samoa (N = 651); Vietnam (N = 499); Samoa (N = 428); Micronesia (N = 285); Hong Kong (N = 247); Tonga (N = 216); Taiwan (N = 170); Marshall Islands (N = 160); Guam (N = 136); other countries with <100 cases each (combined N = 471).