

# Hepatitis B Prevalence and Risk Factors in Foreign-Born Asians and Pacific Islanders at a Federally Qualified Health Center in Hawai‘i, 2015-2020

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## Abstract

The objective of this study was to estimate the prevalence of chronic hepatitis B infection in foreign-born Asians and Pacific Islanders at Kalihi-Palama Health Center in Honolulu, Hawai‘i, and to assess the association between both chronic and resolved hepatitis B infection and risk factors such as household exposure to hepatitis B virus and geographic location of birthplace. The study involved cross-sectional data from 997 participants who accessed medical services at Kalihi-Palama Health Center between September 2015 and July 2020. The prevalence of chronic hepatitis B was 10.7%. On multivariable logistic regression analysis, the adjusted prevalence odds ratio of chronic hepatitis B infection was 3.3 times greater (95% confidence interval: 1.1, 9.2) for those who reported household contact with a person with hepatitis B infection than those who reported no such contact. No association was found with place of birth in this study population. Age was a significant predictor of chronic hepatitis B, with participants between 35-44 years of age having the highest prevalence. Age was also a significant predictor of resolved hepatitis B infection, with participants 65 years of age or older having the highest prevalence. These findings emphasize the need for targeted screening and appropriate follow-up—including vaccination or treatment—in this at-risk population.

## Abbreviations

API = Asian and Pacific Islander  
CDC = Centers for Disease Control and Prevention  
CHB = chronic hepatitis B  
CI = confidence interval  
HCC = hepatocellular carcinoma  
HDOH = Hawai‘i State Department of Health  
HBcAb = hepatitis B core antibody  
HBsAg = hepatitis B surface antigen  
HBV = hepatitis B virus  
HCV = hepatitis C virus  
HIV = human immunodeficiency virus  
KPHC = Kalihi-Palama Health Center  
POR = prevalence odds ratio

## Introduction

In the US, chronic hepatitis B (CHB) infection prevalence is under 1%. Despite making up around 6% of the US population, persons of Asian and Pacific Islander (API) descent are vastly overrepresented, accounting for over 50% of CHB infection cases.<sup>1,2</sup> CHB infection is the leading cause of hepatocellular carcinoma (HCC), accounting for approximately half of all cases globally.<sup>1</sup> Consequently, APIs also have a far greater incidence of HCC than the general population.<sup>3</sup> In endemic regions for hepatitis B, such as East and Southeast Asia, CHB prevalence is high (>8%), and hepatitis B virus (HBV) infection is typically acquired perinatally or in early childhood, leading to a high risk of HCC and progression of chronic infection in 90%

of those infected.<sup>4</sup> In countries where CHB prevalence is low (<2%), HBV infection is typically acquired in adolescence or adulthood percutaneously or sexually, and the risk of progression to chronic infection and HCC is far lower.<sup>4</sup>

Even when an acute hepatitis B viral infection is resolved, there remains a risk for severe disease reactivation for patients. In those with resolved hepatitis B infections, HBV DNA remains in hepatocytes as stable covalently closed circular DNA (ccDNA) and integrated DNA.<sup>5</sup> These patients can be said to be chronically infected, with the infection being under immune control. If these patients undergo immunosuppressive therapy for organ transplantation or cancer, the risk of hepatitis B reactivation can become significant. Coinfection of HBV with HCV or HIV is a risk factor for HBV reactivation even in the absence of immunosuppressive therapy.<sup>6</sup> Previous hepatitis B infection is associated with cirrhosis and HCC in those with non-alcoholic fatty liver disease.<sup>7</sup> Since hepatitis B reactivation can lead to serious health sequelae such as liver failure or even death, education about possible triggers are important for patients with prior exposure, as indicated by positive hepatitis B core antibody lab results.<sup>8</sup>

The concern for CHB and HBV is warranted for Hawai‘i because more than half of the state’s residents identify as API, and about one-fifth of the state’s residents are foreign-born, which is higher than the national average of 13%.<sup>9,10</sup> HBV-associated mortality rates have been consistently higher among API residents in Hawai‘i, compared to rest of the state.<sup>11</sup> HBV infection prevalence among Asian immigrants to the US has been shown to vary by country of origin, with Chinese immigrants, particularly from Fujian province, having the highest prevalence.<sup>12</sup>

The Hawai‘i State Department of Health (HDOH) established the Hawai‘i Enhanced Hepatitis B Screening Program in 2013 to improve screening rates among uninsured foreign-born APIs. An earlier report from this program, covering the period between August 2013 and August 2015, found that self-reported household contact with “someone with hepatitis B” [chronicity of disease not specified] was a significant risk factor for CHB infection.<sup>13</sup> The current study covered the period from September 2015 through July 2020 and sought to identify risk factors for chronic, as well as resolved hepatitis B infections. The findings from this analysis will be used to inform HDOH programs and policies to better allocate resources and target interventions for populations at risk for or living with hepatitis B.

## Methods

### Data Source

The study population consists of adult foreign-born APIs accessing services at the Kalihi-Palama Health Center (KPHC), a federally qualified health center in Honolulu, Hawai‘i, which serves a high-density population of foreign-born APIs at 4 primary clinic sites. Data were retrospectively sourced from the Hawai‘i Enhanced Hepatitis B Screening Program’s risk assessment survey. The survey was originally developed by the Centers for Disease Control and Prevention’s (CDC) Division of Viral Hepatitis and adapted for use by HDOH.<sup>14</sup> The survey was completed by trained KPHC staff, primarily nurses and medical assistants, upon initial intake assessment. The training consisted of initial and ongoing presentations by HDOH staff on basic disease characteristics (eg, transmission, prevention, treatment) and overview of screening form and referral workflow. The survey consisted of 14 questions divided into 3 categories: demographics, medical history, and risk factors. Demographic questions were country of birth, year of birth, sex, race, and ethnicity. Medical history questions included health insurance status, current pregnancy status, hepatitis vaccination status, and HIV status. Risk factors consisted of injection drug use, identification as a male who has sex with males, household contact with a person who has hepatitis B, sexual contact with a person who has hepatitis B, and multiple sex partners. All adult foreign-born APIs accessing services at KPHC between September 2015 and July 2020 were eligible for the survey, regardless of insurance status. HBV serological testing was offered to all eligible participants to detect hepatitis B surface antigen (HbsAg; Elecsys electrochemiluminescence immunoassays; Roche Diagnostics, Indianapolis, IN) and hepatitis B core antibody (HbcAb; Elecsys electrochemiluminescence immunoassays; Roche Diagnostics, Indianapolis, IN).

The study was reviewed by the University of Hawai‘i Institutional Review Board and was deemed “exempt” as it utilized previously collected de-identified data from an ongoing core program of HDOH’s Adult Viral Hepatitis Prevention Program.

### Exposure and Outcome Variables

Exposure variables included age, sex, geographic location of birth, and household contact with hepatitis B. Age in years was treated as a categorical variable with 5 response options: 18-34, 35-44, 45-54, 55-64, and  $\geq 65$  years. Geographic location of birth was also a categorical variable with 4 response options including: Mainland Asia, South/Southeast Asia, Micronesia, and Pacific Islands. Household hepatitis B contact was based on patient self-report of having lived with anyone who has hepatitis B, with the response options *Yes* or *No*. No data was collected from patient on whether household contact had active or resolved hepatitis B. Logistic regression analysis was performed to determine how these exposure variables affected

the outcome variable, which was the HbsAg serological test result, either positive or negative. Unlike its clinical definition, CHB infection was defined as seropositivity for HbsAg, which allowed for simplified analysis and timely response by HDOH program staff.

A second logistic regression analysis was conducted to determine the association between past hepatitis B infection that had resolved, and age, sex, geographic location of birth and household contact with anyone with hepatitis B. A resolved past hepatitis B infection was measured by detection of HbcAb in the absence of HbsAg positivity.

Demographic characteristics for missing data for the HBV exposure variable were tabulated, compared with non-missing data, and found to be similar.

### Statistical Methods

Descriptive and tabular analyses were performed using Microsoft Excel version 16.50.<sup>15</sup> Univariate and multivariable logistic regression analyses were performed using R version 3.6.2.<sup>16</sup> Crude and adjusted prevalence odds ratios (POR) and 95% confidence intervals (CI) were calculated to measure the association between exposure and outcome variables. Previous studies indicate that CHB prevalence is higher in those from high-prevalence countries, men, and older adults. Therefore, geographic location of birth, sex, and age were controlled for in the adjusted model. Reference groups for each variable in the logistic regression models were chosen based on the group with the lowest HbsAg seroprevalence and were kept consistent in the analysis of both chronic and resolved infections.

### Results

Of 997 subjects who participated in the survey, the prevalence of CHB, determined by HbsAg seropositivity, was 10.7% (**Table 1**). Of all participants, 217 (21.8%) selected “Don’t know,” “Decline to answer,” or failed to respond to questions about sex, age, location of birthplace, or household contact with anyone with hepatitis B. The missing data were analyzed and found to be random. These participants were included in the prevalence calculations but were excluded from the regression analyses. The majority of study participants were women (58.2%). Participants’ ages were relatively evenly distributed across the age groups, apart from a limited number of participants over the age of 65 years with a mean and median of 44.5 and 47 years, respectively. Most of the participants were born in Micronesia (53.3%) or South/Southeast Asia (26.2%).

Household hepatitis B contact had a significant association with CHB, adjusted POR 3.3 (95% CI 1.1, 9.2). Age also had a significant association, with the 35-44 year age group having an adjusted POR of 3.1 (95% CI 1.1, 11.0) compared with persons  $\geq 65$  years. Males had a higher prevalence than females,

and participants from Mainland Asia had a higher prevalence than participants from other regions, but differences in sex and geographic location of birth were not statistically significant (Tables 2 and 3).

The prevalence of past infection was 63.5% (Table 1). Age had a significant association with HBcAb seropositivity in the absence of HBsAg positivity. The youngest age groups, 18-34 years and 35-44 years, had adjusted PORs of 0.1 (95% CI 0.1, 0.3) and 0.5 (95% CI 0.3, 0.9), respectively, compared with persons  $\geq 65$  years. Adjusted PORs increased with the age of the participants although only the differences in the 18-34 years and 35-44 years age groups were statistically significant (Table 4).

Table 1. Characteristics of Participants from the Hawai'i Enhanced Hepatitis B Screening Program's Hepatitis B Risk Assessment Survey, September 2015—July 2020 (N = 997)		
Variable	Category	Number (%)
Age group (years)	18-34	227 (22.8)
	35-44	211 (21.2)
	45-54	220 (22.1)
	55-64	224 (22.5)
	>65	115 (11.5)
Race	Asian	431 (43.2)
	Native Hawaiian/Pacific Islander	563 (56.5)
	2 or more races	1 (0.1)
	Unknown	2 (0.2)
Sex	Male	415 (41.6)
	Female	580 (58.2)
	Unknown/No Response	2 (0.2)
Geographic Location of Birthplace	Mainland Asia <sup>a</sup>	149 (14.9)
	South/Southeast Asia <sup>b</sup>	261 (26.2)
	Micronesia <sup>c</sup>	531 (53.3)
	Pacific Islands <sup>d</sup>	56 (5.6)
Insurance	Uninsured	983 (98.6)
	Public	5 (0.5)
	Private	4 (0.4)
	Other	1 (0.1)
	Unknown	4 (0.4)
Household HBV-infection Contact	Yes	18 (1.8)
	No	762 (76.4)
	Unknown/No Response	217 (21.8)

Sexual Contact with an HBV-infected Person	Yes	22 (2.2)
	No	842 (84.5)
	Unknown/No Response	133 (13.3)
HIV+	Yes	3 (0.3)
	No	905 (90.8)
	Unknown/No Response	89 (8.9)
Injection Drug Use	Yes	7 (0.7)
	No	970 (99.3)
Male Sex with Male	Yes	5 (0.5)
	No	387 (38.8)
	Unknown/No Response	605 (60.7)
Multiple Sex Partners	Yes	24 (2.4)
	No	848 (85.1)
	Unknown/No Response	125 (12.5)
HBsAg Test Result	Positive	107 (10.7)
	Negative	890 (89.3)
HBcAb Test Results	Positive	633 (63.5)
	Negative	364 (36.5)
HBcAb Test Results among HBsAg Seronegative Persons (n=890)	Positive	526 (59.1)
	Negative	364 (40.9)

<sup>a</sup> Mainland Asia includes: China (n=117), Japan (n=2), South Korea (n=28), Taiwan (n=1), Mongolia (n=1)

<sup>b</sup> South/Southeast Asia includes: Bangladesh (n=2), Cambodia (n=2), Laos (n=3), Philippines (n=155), Myanmar (n=5), Thailand (n=6), Vietnam (n=88),

<sup>c</sup> Micronesia includes: Federated States of Micronesia (n=410), Republic of Marshall Islands (n=121)

<sup>d</sup> Pacific Islands includes: American Samoa (n=7), Fiji (n=1), Guam (n=4), Northern Mariana Islands (n=1), Samoa (n=20), Tonga (n=22)

**Table 2. Characteristics of Participants from the Hawai'i Enhanced Hepatitis B Screening Program's Risk Assessment Survey with and without HBsAg Seropositivity, September 2015–July 2020 (N=997)**

Variable of Interest	HBsAg- (%)	HBsAg+ (%)	Unknown (%)
<b>Age Group (years)</b>			
18-34	200 (88.1)	26 (11.5)	1 (0.4)
35-44	181 (85.8)	29 (13.7)	1 (0.5)
45-54	192 (88.1)	26 (11.9)	2 (0.9)
55-64	204 (91.1)	20 (8.9)	0
>65	109 (94.8)	6 (5.2)	0
<b>Sex</b>			
Male	365 (88.0)	48 (11.6)	2 (0.5)
Female	519 (89.5)	59 (10.2)	2 (0.3)
<b>Geographic Location of Birthplace</b>			
Mainland Asia <sup>a</sup>	119 (79.9)	29 (19.5)	1 (0.7)
South/Southeast Asia <sup>b</sup>	241 (92.3)	17 (6.5)	3 (1.1)
Micronesia <sup>c</sup>	472 (88.9)	59 (11.1)	0
Pacific Islands <sup>d</sup>	54 (96.4)	2 (3.6)	0
<b>Household HBV-infection contact</b>			
Yes	12 (66.7)	6 (33.3)	0
No	680 (89.2)	79 (10.4)	3 (0.4)

<sup>a</sup> Mainland Asia includes: China (n=117), Japan (n=2), South Korea (n=28), Taiwan (n=1), Mongolia (n=1)

<sup>b</sup> South/Southeast Asia includes: Bangladesh (n=2), Cambodia (n=2), Laos (n=3), Philippines (n=155), Myanmar (n=5), Thailand (n=6), Vietnam (n=88)

<sup>c</sup> Micronesia includes: Federated States of Micronesia (n=410), Republic of Marshall Islands (n=121)

<sup>d</sup> Pacific Islands includes: American Samoa (n=7), Fiji (n=1), Guam (n=4), Northern Mariana Islands (n=1), Samoa (n=20), Tonga (n=22)

**Table 3. Crude and Adjusted Prevalence Odds Ratios and 95% Confidence Intervals of CHB Infection among Participants from the Hawai'i Enhanced Hepatitis B Screening Program's Hepatitis B Risk Assessment Survey, September 2015—July 2020**

Predictor Variable	HBsAg Seropositivity Crude Association		HBsAg Seropositivity Adjusted Association	
	POR	95% CI	POR	95% CI
<b>Household HBV-infection Contact</b>				
Yes	4.3*	(1.5, 11.5)	3.3*	(1.1, 9.2)
No	Ref	Ref	Ref	Ref
<b>Age Group (years)</b>				
18-34	2.3	(1.0, 6.5)	2.6	(0.9, 9.2)
35-44	2.9*	(1.2, 7.9)	3.1*	(1.1, 11.0)
45-54	2.4	(1.0, 6.7)	2.7	(1.0, 9.5)
55-64	1.8	(0.7, 5.0)	2.4	(0.8, 8.6)
>65	Ref	Ref	Ref	Ref
<b>Sex</b>				
Male	--	--	1.3	(0.8, 2.1)
Female			Ref	Ref
<b>Geographic Location of Birthplace</b>				
Mainland Asia <sup>a</sup>	--	--	3.7	(1.0, 24.3)
Micronesia <sup>b</sup>			2.3	(0.7, 14.5)
South/Southeast Asia <sup>c</sup>			1.2	(0.3, 7.8)
Pacific Islands <sup>d</sup>			Ref	Ref

\*Statistically significant finding ( $P < .05$ )

<sup>a</sup> Mainland Asia includes: China, Japan, South Korea, Taiwan, Mongolia

<sup>b</sup> Micronesia includes: Federated States of Micronesia, Republic of Marshall Islands

<sup>c</sup> South/Southeast Asia includes: Bangladesh, Cambodia, Laos, Philippines, Myanmar, Thailand, Vietnam,

<sup>d</sup> Pacific Islands includes: American Samoa, Fiji, Guam, Northern Mariana Islands, Samoa, Tonga

**Table 4. Prevalence, Crude, and Adjusted Prevalence Odds Ratios and 95% Confidence Intervals of Past HBV Infection Among HBsAg seronegative Participants From the Hawai'i Enhanced Hepatitis B Screening Program's Hepatitis B Risk Assessment survey, September 2015—July 2020**

Predictor Variable	HBcAb Seropositivity Crude Association		HBcAb Seropositivity Adjusted Association	
	POR	95% CI	POR	95% CI
<b>Age Group (years)</b>				
18-34	0.2*	(0.1, 0.3)	0.1*	(0.1, 0.3)
35-44	0.6*	(0.4, 1.0)	0.5*	(0.3, 0.9)
45-54	0.8	(0.5, 1.4)	0.7	(0.4, 1.2)
55-64	0.8	(0.5, 1.4)	0.8	(0.4, 1.3)
>65	Ref	Ref	Ref	Ref
<b>Geographic Location of Birthplace</b>				
Mainland Asia <sup>a</sup>	--	--	1.2	(0.6, 2.7)
Micronesiab			1.3	(0.6, 2.6)
South/Southeast Asia <sup>c</sup>			0.6	(0.3, 1.2)
Pacific Islands <sup>d</sup>			Ref	Ref
<b>Sex</b>				
Male	--	--	1.3	(1.0, 1.8)
Female			Ref	Ref
<b>Household HBV-infection Contact</b>				
Yes	--	--	1.2	(0.4, 4.3)
No			Ref	Ref

\*Statistically significant finding ( $P < .05$ )

<sup>a</sup> Mainland Asia includes: China, Japan, South Korea, Taiwan, Mongolia

<sup>b</sup> Micronesia includes: Federated States of Micronesia, Republic of Marshall Islands

<sup>c</sup> South/Southeast Asia includes: Bangladesh, Cambodia, Laos, Philippines, Myanmar, Thailand, Vietnam,

<sup>d</sup> Pacific Islands includes: American Samoa, Fiji, Guam, Northern Mariana Islands, Samoa, Tonga

## Discussion

This study found the prevalence of CHB, as determined by HBsAg seropositivity, from 2015 to 2020 to be 10.7%, which is much higher than the estimated prevalence for the general US and for many global regions.<sup>17</sup> A previous study by Ferrer, et al, among KPHC patients sampled from 2013-2015, found a lower (but still high) prevalence of CHB (5.6%).<sup>12</sup> The increased prevalence of CHB in the current study could be explained by the age-distribution of the populations sampled in the 2 studies. The current study includes a much younger population compared with that sampled by Ferrer et al, and younger age was associated with higher prevalence of CHB in both studies.<sup>13</sup> Notably, the proportion of past HBV infection was similar between the Ferrer, et al, study (58.5%) and this analysis (63.5%).<sup>13</sup>

Similar to previous findings, household contact with HBV was found to be a significant predictor of CHB. While Ferrer et al reported a prevalence ratio of 6.0 for household contact with

HBV compared with a POR of 3.3 in the current study, the 95% confidence intervals in both studies are wide and overlap.<sup>13</sup> These findings align with CDC recommendations to protect household contact of persons living with HBV by ensuring timely screening and appropriate immunizations.<sup>18</sup> Since federally qualified health centers like KPHC can provide culturally appropriate, in-language primary care services for foreign-born families and households, these findings reaffirm the importance of integrating HBV services in community-based health care settings.

Age was also found to be a significant predictor of CHB, with the 35-44 year age bracket having the highest adjusted POR. The lower prevalence in the 18-34 year age group may be explained by higher vaccination rates. For example, the Federated States of Micronesia, birthplace of over half of the study participants, incorporated routine HBV vaccination in its pediatric program in 1988.<sup>19</sup> The lower CHB prevalence in participants over the age of 45 years may partially be due to seroclearance of HBsAg, which occurs at a rate of 1% annually.<sup>20</sup> In the Ferrer study, age was not found to be a significant predictor of CHB, which could possibly be due to the older study population; 20.9% of the participants in the Ferrer, et al study were over the age of 65 years, compared to 11.5% in this study.

Age was also a significant predictor of past HBV infection, with the 2 youngest age groups having significantly lower prevalence. Since HBV vaccination became required for native born and foreign-born children in Hawai'i in 1998, lower prevalence in younger populations is expected.<sup>21</sup> Even in those with HBsAg seroclearance, an age greater than 50 years at the time of seroclearance has been shown to be a significant risk factor for HCC development.<sup>22</sup> Those with past HBV infection remain at risk of reactivation and should be screened prior to immunosuppressive therapy.<sup>23</sup>

Finally, no significant findings were related to place of birth, which was surprising given the varying CHB prevalence among the different home countries found in prior literature.<sup>14</sup> These findings may be explained by the results of a 2021 metanalysis, which found CHB prevalence in emigrants can differ from CHB prevalence in in-country populations. In particular, emigrants from China had higher prevalence than native Chinese, whereas emigrants from Micronesia had lower prevalence than native Micronesians.<sup>24</sup> Therefore, even though prevalence in home countries varies, country of origin may not always be a statistically significant predictor of CHB prevalence in emigrant populations. As such, the HDOH should continue to support the screening program for foreign born Asians and Pacific Islanders. However, it is unclear if there are additional populations that could benefit from HBV screening based on this study.

## Limitations

There were several limitations to the study. CHB infection was defined as a single positive serological test for HBsAg instead

of multiple persistent positive results. Even though it is possible that adults with isolated HBsAg positivity had acute infections, it is unlikely because perinatal and childhood infections are the predominant source of any hepatitis B infection among foreign-born APIs.<sup>25</sup> Due to the cross-sectional study design, causal inferences and temporal associations between exposure and outcome could not be made. Since all the participants were already accessing services at KPHC, the sample is not representative of the general population. The quality of the data may have been affected by language barriers between patients and health center staff, which were addressed by using in-language materials and language-specific community health workers. The low numbers of persons reporting household contact led to wide confidence intervals. Patients may not have been aware of the hepatitis B history of household contacts, which was not verified by additional testing. Verification of the hepatitis B history of household contacts through testing would also provide more valid data than self-reports. The large numbers of nonresponses constitute an additional limitation. Other risk factors for hepatitis B include sexual contact with an HBV infected person, HIV infection, injection drug use, male sex with males, and multiple sexual partners. These variables were included in the survey, but due to missing data from nonresponses, they were excluded from regression analyses. Also, the number of eligible patients who declined to participate was not collected.

## Conclusion

The adjusted POR of CHB infection was 3.3 times greater for those who reported household contact with a person with chronic hepatitis B infection than those who reported no such contact. The high prevalence associated with household contact underscores the need for testing and vaccination of household members of individuals with CHB infection.

Due to the small sample size for some of the variables, such as number of people who reported household contact with an HBV-infected person, further studies should include expanding screening for and analysis of CHB across multiple health centers and in nonclinical settings. More data is required for thorough analyses of the impact of risk factors other than household exposure.

## Conflict of Interest

None of the authors identify a conflict of interest.

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