RESEARCH COMMUNICATION

Stopping a Silent Killer in the Underserved Asian and Pacific Islander Community: A Chronic Hepatitis B and Liver Cancer Prevention Clinic by Medical Students

Steven Y Lin[1-3]*, Ellen T Chang[3-5], Samuel K So[1-4]

Abstract

Objectives: To assess and alleviate the burden of chronic hepatitis B virus (HBV) infection among low-income, uninsured Asian and Pacific Islanders (APIs) in San Jose, California. Methods: From 2007 to 2008, we provided free HBV testing and follow-up to 510 patients, 74% of whom were foreign-born Vietnamese. Patients were tested for hepatitis B surface antigen and surface antibody. Chronically infected patients who elected to undergo follow-up monitoring were evaluated for liver damage (ALT), liver cancer (AFP), and HBV replication (HBV DNA). Results: Overall, 17% were chronically infected; 33% of these were unaware that they were infected. Of those who underwent follow-up monitoring, 100% had elevated ALT, 9% had elevated AFP, and 24% had HBV DNA levels that exceeded the threshold for treatment. Patients who were candidates for antiviral therapy were enrolled in drug assistance programs, and those with elevated AFP levels were referred for CT scans. Uninfected patients lacking protective antibodies were provided free HBV vaccinations. Conclusions: More liver cancer prevention in the medically underserved API community is needed, including universal screening for HBV and follow-up for those chronically infected.

Key Words: Asian and Pacific Islanders - chronic hepatitis B - liver cancer - prevention clinic

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Introduction

Chronic hepatitis B virus (HBV) infection is a serious liver disease that causes a disproportionate burden of morbidity and premature death among Asian and Pacific Islanders (APIs) in the U.S. (Chang et al., 2007). Without early detection, routine monitoring or timely treatment, chronic HBV infection confers a 25% risk of death from cirrhosis or liver cancer (WHO, 2008). This under-recognized public health problem is most urgent among immigrants from East Asia, Southeast Asia, and the Pacific Islands, where chronic HBV infection is endemic, with an estimated prevalence of 2.4%-16.0% (Custer et al., 2004). In the U.S., it is estimated that around 1 in 10 APIs, particularly the foreign-born, are chronically infected with HBV (Lin et al., 2007).

Most APIs who are chronically infected with HBV acquire their infection at birth through mother-to-child transmission or during childhood, which puts them at a 200-fold greater risk of developing liver disease than those who are uninfected (Jenkins et al., 2001; Beasley et al., 1981). Among all major racial/ethnic groups in the U.S., only APIs suffer cancer as the leading cause of death (NCHS, 2005). Although liver cancer is relatively rare in the U.S., it is the second most common cause of cancer death in API men (USCSWG, 2005). Despite medical advances, the overall 5-year survival rate of liver cancer remains below 10% (Jemal et al., 2004), stressing the need for preventive action, especially for underserved immigrants with poor access to regular health care.

Since most liver cancer cases in APIs are caused by chronic HBV infection (Hwang et al., 1996) and because patients with chronic HBV infection are usually asymptomatic until they develop advanced liver disease (Wright, 2006), community prevention programs should include HBV screening for all APIs, vaccination for those who lack protective antibodies, and routine monitoring for liver function and liver cancer for those who are chronically infected. We recently showed that universal HBV screening combined with treatment of those chronically infected is a cost-effective strategy to reduce the burden of liver disease in APIs (Hutton et al., 2007). To implement such a program, we founded a non-profit clinic in one of the largest API communities in the U.S.: San Jose, California (USCB, 2008).

Materials and Methods

The Hep B Free Clinic is a medical student-run grassroots organization that focuses on HBV and liver

*[1]School of Medicine, Stanford University, [2]Hep B Free Clinic, San Jose, [3]Asian Liver Center, Stanford University, [4]Stanford Cancer Center, Stanford, [5]Northern California Cancer Center, Fremont, California, USA *For Correspondence: linsteve@stanford.edu*

cancer prevention in the underserved API immigrant community of San Jose, California. On every Saturday between July 2007 and July 2008, we provided free HBV screening, vaccination and monitoring of chronic infection to individuals with low income, poor access to health care, and minimal English proficiency. Patients learned about our program via Vietnamese, Chinese, and English advertisements in newspapers and on radio and television.

Of the 510 patients served, ages ranged from 16 to 86 (median = 54 years; 63% were 50 years or older); 54% were female and 46% male (Table 1). The majority (96%) were born in Vietnam, China, or other Asian countries. Nearly one-third (30%) of the patients immigrated to the U.S. less than ten years ago, and most (94%) spoke a primary language other than English. Although the Hep B Free Clinic specifically targeted high-risk API immigrants in San Jose (which has the third largest API population in the U.S.) (USCB, 2008), we welcomed patients from 30 other cities in the San Francisco Bay Area (76% living in San Jose; 93% living within 20 miles of San Jose), as well as non-API members of the community. At the time of registration, patients completed a survey (written in Vietnamese, Chinese, and English) that assessed their demographic information, personal or family history of chronic HBV infection or liver cancer, and HBV vaccination status (Table 2). Of those patients who provided insurance information, 75% had no health insurance at enrollment. All patients provided written informed consent to participate in this study, which was approved by the Stanford Institutional Review Board.

Patients were screened for HBV by venipuncture, and blood samples were tested at the Stanford Hospital Clinical Laboratories for hepatitis B surface antigen (HBsAg) and surface antibody (anti-HBs). Since most APIs are infected with HBV during birth or early childhood, all those who tested positive for HBsAg were considered to be chronically infected (Shepard et al., 2006). For those who elected to undergo follow-up monitoring, a series of blood tests were administered to evaluate for liver damage (alanine transaminase, ALT), liver cancer (alpha-fetoprotein, AFP), HBV replication (hepatitis B e antigen, hepatitis B e antibody, and HBV DNA by PCR), and hepatitis A virus (HAV) antibodies (to assess need for HAV vaccination, which was offered at no cost to those who tested negative for anti-HAV). Elevated ALT was defined as >30 IU/ml for men, >19 IU/ml for women; elevated AFP was defined as >10 IU/ml; and elevated HBV DNA as >20,000 copies/ml, the American Association for the Study of Liver Disease criterion for starting treatment (Lok and McMahon, 2007). Patients who tested negative for HBsAg and anti-HBs were considered as unprotected against HBV, and were offered free HBV vaccines provided by the California Department of Health Services and the Asian Liver Center at Stanford University. Patients who tested negative for HBsAg and positive for anti-HBs were considered as immune. We compared differences in patient characteristics by HBV infection status (chronically infected or unprotected versus immune) using multivariable logistic regression, adjusting for age, sex, and race/ethnicity.

Table 1. Participant Demographic Characteristics Overall and by Hepatitis B Virus (HBV) Status

HBV status Characteristic	Total (510)	Infected* (87)	UP[1] (144)	Immune[2] (279)
Age group (years)				
<30	53 (10)	7 (8)	12 (8)	34 (12)
30-39	55 (11)	16 (18)	12 (8)	27 (10)
40-49	82 (16)	14 (16)	20 (14)	48 (17)
50-59	165 (32)	31 (36)	54 (38)	80 (29)
60-69	122 (24)	17 (20)	34 (24)	71 (25)
≥70	33 (6)	2 (2)	12 (8)	19 (7)
Median (years)	54	53	55	54
Sex				
Male	237 (46)	53 (61)	59 (41)	125 (45)
Female	273 (54)	34 (39)	85 (59)	154 (55)
Race/ethnicity				
Vietnamese	370 (73)	58 (67)	100 (69)	212 (76)
Chinese	120 (24)	25 (29)	33 (23)	62 (22)
Other Asian	11 (2)	2 (2)	6 (4)	3 (1)
Non-Asian	9 (2)	2 (2)	5 (3)	2 (1)
Country of birth				
Vietnam	376 (74)	59 (68)	104 (72)	213 (76)
China	69 (14)	17 (20)	15 (10)	37 (13)
Other Asian	43 (8)	8 (9)	15 (10)	20 (7)
USA	14 (3)	2 (2)	5 (3)	7 (3)
Other country	8 (2)	1 (1)	5 (3)	2 (1)
Years since immigration				
<5	89 (18)	5 (6)	10 (7)	20 (7)
5-9	60 (12)	19 (22)	26 (19)	58 (21)
10-14	70 (14)	19 (22)	37 (27)	66 (24)
15-19	122 (25)	9 (11)	18 (13)	43 (16)
20-29	103 (21)	12 (14)	12 (9)	36 (13)
≥30	35 (7)	19 (22)	29 (21)	41 (15)
Born in USA	14 (3)	2 (2)	5 (4)	7 (3)
Missing	17	2	7	8
Median (years)	15	15	15	15
Primary language				
Vietnamese	361 (71)	56 (64)	102 (71)	203 (73)
Mandarin	84 (16)	13 (15)	22 (15)	49 (18)
Cantonese	22 (4)	10 (11)	4 (3)	8 (3)
Other Asian	7 (1)	2 (2)	3 (2)	2 (1)
English	30 (6)	6 (7)	9 (6)	15 (5)
Iberian	6 (1)	0 (0)	4 (3)	2 (1)
City of residence				
San Jose	387 (76)	58 (67)	107 (74)	222 (80)
≤20 miles	86 (17)	15 (17)	26 (18)	45 (16)
>20 miles	37 (7)	14 (16)	11 (8)	12 (4)

*HBsAg-positive; UP[1], unprotected, HBsAg-negative, anti-HBs)-negative; [2]HBsAg-negative, anti-HBs-positive

Results

Of the 510 individuals screened, 17% were chronically infected with HBV (Table 2), including 16% of Vietnamese, 21% of Chinese, 18% of other Asians and 22% of non-Asians. Remarkably, up to one-third (33%) of those chronically infected were unaware that they were infected; nearly one-quarter (22%) reported that they had never been diagnosed with chronic HBV infection, whereas 11% either did not know or did not report whether they had been previously diagnosed. When we excluded the 58 individuals who reported having been previously diagnosed with chronic HBV infection, 6% (29 of 452) of the previously undiagnosed patients were found to be chronically infected with HBV. Of the patients who

Table 2. Participant Demographic Characteristics Overall and by Hepatitis B Virus (HBV) Status

HBV status Characteristic	Total (510)	Infected* (87)	UP[1] (144)	Immune[2] (279)
Ever previously tested for hepatitis B				
No	270 (53)	18 (21)	82 (57)	170 (61)
Yes	139 (27)	63 (72)	23 (16)	53 (19)
Don't know[#]	101 (20)	6 (7)	39 (27)	56 (20)
Ever told by a doctor that you have hepatitis B				
No	329 (65)	19 (22)	101 (70)	209 (75)
Yes	71 (14)	58 (67)	5 (3)	8 (3)
Don't know[#]	110 (22)	10 (11)	38 (26)	62(22)
Ever received vaccination shots for hepatitis B				
No	314 (62)	74 (85)	85 (59)	155 (56)
Yes	66 (13)	4 (5)	16 (11)	46 (16)
Don't know[#]	130 (25)	9 (10)	43 (30)	78 (28)
Any family member with hepatitis B				
No	276 (54)	37 (43)	86 (60)	153 (55)
Yes	100 (20)	33 (38)	19 (13)	49 (18)
Don't know[#]	133 (26)	17 (20)	39 (27)	77 (28)
Any family member with liver cancer				
No	390 (76)	67 (77)	106 (74)	216 (77)
Yes	11 (2)	2 (2)	2 (1)	7 (3)
Don't know[#]	109 (21)	18 (21)	35 (24)	56 (20)
Currently have health insurance				
No	363 (75)	71 (86)	94 (71)	198 (74)
Yes	119 (25)	12 (14)	39 (29)	68 (26)
Missing	28	4	11	13
Household size				
1	53 (11)	11 (13)	12 (9)	30 (11)
2	115 (24)	22 (26)	27 (20)	66 (25)
3	119 (24)	21 (25)	38 (28)	60 (22)
4	98 (20)	19 (22)	21 (15)	58 (22)
≥5	104 (21)	12 (14)	38 (28)	54 (20)
Missing	21	2	8	11
Alanine aminotransferase level (IU/ml; HBsAg-positive only)				
21-49	---	38 (56)	---	---
50-99	---	22 (32)	---	---
≥100	---	8 (12)	---	---
Missing	---	19	---	---
Alpha-fetoprotein level (IU/ml; HBsAg-positive only)				
None	---	18 (27)	---	---
2-9	---	43 (64)	---	---
_10	---	11 (16)	---	---
Missing	---	20	---	---
Hepatitis B e antigen status (HBsAg-positive only)				
Negative	---	36 (86)	---	---
Positive	---	6 (14)	---	---
Missing	---	45	---	---
HBV DNA level (IU/ml; HBsAg-positive only)				
None	---	10 (22)	---	---
6-999	---	13 (29)	---	---
1,000-19,999	---	11 (24)	---	---
≥20,000	---	11 (24)	---	---
Missing	---	42	---	---
Hepatitis A total antibody status (HBsAg-positive only)				
Negative	---	5 (8)	---	---
Positive	---	55 (92)	---	---
Missing	---	27	---	---

*HBsAg-positive; UP[1], unprotected, HBsAg-negative, anti-HBs-negative; [2]HBsAg-negative, anti-HBs-positive; [#] or missing

elected to undergo follow up monitoring for chronic HBV infection, 100% (68 of 68) showed signs of active liver damage as indicated by elevated ALT. Of the same patients, 9% showed elevated AFP, the most commonly used test to screen for liver cancer. Nearly one-quarter (24%) of those chronically infected had a viral load of over 20,000 copies/ml, exceeding the threshold for antiviral treatment. Patients who were candidates for antiviral therapy were signed up for free patient drug assistance programs, and those requiring triphasic CT scans for possible liver cancer were referred to a gastroenterologist at the neighboring Santa Clara Valley Medical Center.

Overall, 28% of the 510 patients lacked protective antibodies against HBV and were therefore susceptible to future infection (Table 2). Remarkably, only 13% of all patients reported having been vaccinated against HBV. Of those who reported having been vaccinated, 11% lacked protective antibodies and 5% were found to be chronically infected with HBV. All unprotected patients were offered free HBV vaccines. In addition, all chronically infected patients who lacked protective antibodies against HAV were offered free HAV vaccines to reduce the chance of further liver damage (ALC, 2007).

Discussion

Our findings from the Hep B Free Clinic underscore the enormous yet hidden burden of chronic HBV infection among API immigrants. This is true especially among foreign-born Vietnamese (74% of our patients), who are particularly underserved and understudied. Our results showing HBV seroprevalence of 17% among predominantly foreign-born APIs, and 6% among those previously undiagnosed with the infection, are consistent with previous reports (Chao et al., 2004; Guane et al., 2004; CDC, 2006; Lin et al., 2007). We also show for the first time that virtually all of those chronically infected with HBV in this population had active liver damage despite the lack of symptoms, and 9% had elevated AFP, a screening test for liver cancer. Even though nearly 1 in 4 of those chronically infected had a viral load that exceeded the criterion for treatment, none of our chronically infected patients were currently on antiviral therapy, and as many as 1 in 3 of them were unaware that they were infected.

This lack of awareness and treatment carries life-threatening implications for all APIs, because undetected and unmanaged chronic HBV infection is associated with a 25% risk of death from cirrhosis or liver cancer, and can also be unknowingly transmitted to close contacts. We also showed that only 13% of the study population reported having been vaccinated against HBV. Furthermore, among those who said they were vaccinated, 1 in 10 lacked protective antibodies, and 1 in 20 was chronically infected, again confirming previous studies (Lin et al., 2004). Our striking findings call for more widespread preventive work in this community, including universal screening of all foreign-born API adults regardless of their vaccination status, as recommended by the U.S. Advisory Committee on Immunization Practices (Mast et al., 2006; Lin et al., 2007).

One limitation of our study is its non-random recruitment of participants, so the findings may not be generalizable to the entire API population. Also, the

prevalence of chronic HBV infection was likely overestimated given that many participants already knew they were infected. However, when all patients who reported having been previously diagnosed with chronic HBV infection were excluded, 6% were still found to be chronically infected with HBV, which is consistent with previous reports (Lin et al., 2007). One major strength of our study is that, to our knowledge, it was the first to examine the prevalence of elevated liver enzymes (ALT) and performed a screening test for liver cancer (AFP) among API immigrants with chronic HBV infection.

Given the high prevalence of chronic HBV infection, particularly undetected infection, among APIs, more community-based programs that promote universal HBV screening and vaccination are needed in places such as New York City and Los Angeles, which have the largest API populations in the U.S., and the San Francisco Bay Area and Honolulu, which have the highest percentages of APIs (USCB, 2008). Innovative partnerships between public health institutions, non-profit organizations, and academic centers, like those supported by the Hep B Free Clinic, are key to successful interventions in this population. Such programs are highly cost-effective public health strategies to reduce the disproportionate burden of cirrhosis and liver cancer in the API community (Hutton et al., 2007), especially for immigrants with little access to regular health care.

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