

Update on the Recommended HBV Screening in the United States

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Abstract

Hepatitis B virus (HBV) infection is a serious public health problem that can be associated with HBV-cirrhosis and hepatocellular carcinoma (HCC). HBV-related chronic liver disease is particularly prevalent in the Asian population with significant disparity. Although convenient HBV screening and diagnosis tests are safe and effective, HBV vaccination have been available for many years, under-screening and under-diagnosis of HBV infection is still a serious problem in the USA and worldwide. This article systemically reviewed effectiveness of universal HBV vaccination programs that have been implemented in many countries and regions, the facts of HBV under-screening in the U.S., especially in Asian Americans, and the updated recommendations of HBV screening and vaccination by Center of Disease Control and Prevention (CDC).

[*NA J Med Sci. 2011;4(1):18-22.*]

Key Words: *Hepatitis B Virus (HBV), HBV Screening, hepatitis B, Asian Americans*

Received 11/17/2010; Revised 01/07/2011; Accepted 01/10/2011

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Hepatitis B virus (HBV) infection is one of the most common infectious diseases globally, and a severe threat to the human health. Approximately 350 to 400 million people worldwide are chronic infected by HBV. Chronic HBV infection causes chronic hepatitis B (CHB) that is associated with cirrhosis and hepatocellular carcinoma (HCC).^{1,2} Approximately 0.5-1.2 million deaths are attributed to HBV infection annually.² Worldwide, HBV infection causes up to 80 percent of HCC, one of the most lethal and fastest growing cancers.^{1,2,9}

HBV infection is now preventable and treatable. However, as patients with HBV infection are usually asymptomatic, many of these individuals are unaware of such infection, or have not sought medical care due to many reasons or barriers. As a result, diagnosis of CHB can be delayed, or made after development of CHB related complications. Public unawareness, cultural barriers, and lacking healthcare resource are common challenges in the battle against HBV screening, and access to HBV-related care.

Prevalence of HBV Infection in the US and Its Health Care Burden in Asian Americans

It is known that HBV infection has a remarkable racial disparity. In the United States, it is estimated that 1.4 million people are infected by HBV and notably, more than half of those are Asian Americans and Native Hawaiian and Other Pacific Islanders. Approximately 1 in 10 Asian Americans are chronically infected with HBV³⁻⁵ compared to 1 in 1,000 ratio of HBV infection in the general population of the United States.⁶ There are more than 43,000 new cases infected by HBV in United States each year, with the greatest incidence among adults between ages 19-49 years old.⁷ HBV infection is one of the leading health disparities between Asians and non-Hispanic whites.

The predominant routes of transmission vary according to the endemicity of the HBV infection. In areas with high HBV endemicity, perinatal transmission is the main mode of transmission, whereas in areas with low HBV endemicity, sexual contact amongst high-risk adults is the predominant mode. HBV has been classified into 8 genotypes, i.e. A to H, based on the divergence of the entire genome sequence. HBV genotypes have distinct geographical distributions.⁸

In most parts of Asia, the HBsAg carrier rate in the general population is approximately 5% to 20%.⁹ HBV infection causes 60% to 80% of the primary liver cancer worldwide, accounting for 1 of 3 major cancer deaths in Asia, the Pacific

Rim, and Africa. Asian Americans not only have the highest rates of CHB among all racial/ethnic groups in the United States, but also have a disproportionately high risk for HCC. HBV-related mortality among Asian Americans and Native Hawaiian and other Pacific Islanders is seven times greater than the rate among whites.¹⁰⁻¹¹ This is strongly supported by the fact that San Francisco has the highest HCC rate in the country, mostly due to the city's large population of Asian-Americans, in whom HBV infection has been an epidemic.

Clearly, HBV and HCC are becoming an Asian-American epidemic and huge healthcare burden. To combat this epidemic, it is crucial to have an effective hepatitis B screening program in primary care setting and community outreach systems. This would result in early identification those silently infected individuals, and to allow for the implementation of effective treatment programs, utilizing prevention and monitoring strategies to reduce HBV prevalence, improve access to HBV care, and minimize HBV-related mortality from HBV related complications, such as cirrhosis and HCC.

HBV Vaccination Is Effective in Preventing HBV Infection

The goals of HBV screening and universal HBV vaccination mainly include the following: first of all, provide universal protection, and eradicate HBV infection; secondly, identify the HBV cases for education and prevent transmission, and thirdly, provide HBV treatment when needed.¹²⁻¹³ Many studies have demonstrated that universal HBV vaccination can effectively reduce the prevalence of both HBV infection and HCC. Thus, HBV vaccine has been described as the first effective anticancer vaccine, and its use has been promoted by the World Health Organization (WHO) as a routine care worldwide since 1997.

HBV universal vaccination of newborns was initiated in 1984 in Taiwan. Ni et al.¹⁴ reported 80% reduction of HBV infection by 1994 and 90% reduction of the infection rate by 1999 in Children in Taiwan. Chang et al. published their findings in 1997,¹⁵ which confirmed that the annual incidence of HCC dropped nearly 50% from 1990 to 1994 after universal vaccination of newborns initiated in 1986.

In 1992 the health authority in China recommended HBV vaccinating for all infants. The overall coverage of hepatitis B vaccine in infants has increased steadily to more than 95.0% in urban and 83.0%–97.0% in rural areas. As a result, chronic HBV carrier rate in children <10 years of age was decreased from 10.0% before the mass vaccination to 1.0%–2.0% in 2006. In general population it was decreased from 10.0% to 7.2%. It is estimated that the nationwide mass hepatitis B vaccination has reduced more than 30 million of chronic HBV infections and HBV related severe sequelae in China.¹⁶ Three main strategies have been proved to be effective in preventing HBV infection in China.¹⁸ They are behavior modification, passive immunoprophylaxis, and active immunization.

The prevalence of HBV carriers in Korea was also markedly reduced after the introduction of the universal HBV vaccination program. Korea is now classified as an area of intermediate endemicity for HBV.¹⁷ Wasley et al. reported that HBV prevalence has also been decreased among US children thanks to the global and domestic vaccination.¹⁹

Chen analyzed the major approaches available in controlling HBV infection and found that HBV vaccination can effectively preclude HBV infection, particularly for pre-exposure prophylaxis. HBV treatments, such as pegylated interferon or nucleos(t)ide analogs, can be effective and produce satisfactory outcomes, but chronic carriage of HBV is not easy to eliminate. Their data further support the value of universal HBV vaccination of the newborns.²

Studies have demonstrated that the universal HBV vaccination is cost-effective. Hutton and colleagues conducted an analysis on cost effectiveness of four HBV screening and vaccination strategies. They concluded that free nationwide catch-up hepatitis B vaccination program for unvaccinated children and adolescents aged 1 to 19 years in China, in addition to ongoing efforts to improve birth dose and newborn vaccination coverage, will be cost-saving and can generate significant population-wide health benefits. The success of such a program in China could serve as a model for other endemic countries.²⁰

Under Diagnosis of HBV Infection in the United States

A recent Institute of Medicine (IOM) report systematically reviewed the current diagnosis and control approaches to HBV infection in the U.S. They concluded HBV is the world's most common and serious human viral infection that it is highly prevalent in Asian population. However, up to two thirds of those Asian Americans with HBV infection are unaware their condition. Under diagnosis of HBV is a serious problem, due to many barriers of prevention and care mainly inadequate attention and effort from health agents and patients.²¹

Many barriers can negatively impact the implement of HBV screening and vaccination, especially in Asian Americans. Unlike most other serious diseases, HBV infection usually does not present obvious symptoms until its final stages which involve often fatal complications. It is for these features that HBV is considered a "silent killer". This long-term latency could significantly reduce patients', public, and even health providers' awareness.²²⁻²⁶

Within Asian community (one of the fastest growing and most diverse populations in the United States²⁸), knowledge about HBV is very limited,^{24-25,28-29} and no effective prevention and screening service is established.³⁰⁻³¹ One study indicated that less than one-half of Chinese in the US Pacific Northwest have been tested for hepatitis B and, only 20% of the individuals had ever received a physician's recommendation for HBV testing. A small portion of respondents (21%) had asked a physician for testing and of

those only 88% of them had actually received testing, indicating that some physicians discourage testing among individuals who requests it.³¹

On the other hand, the HBV screening guidelines have been at least in part overlooked by clinicians. Up to two thirds of Asian Americans chronically infected with hepatitis B are unaware that they are affected and, therefore have limited motivation to seek medical assistance.³¹ The additional barriers are high uninsured rate, financial hardship, as well as language and cultural barriers. It is noticeable that 21% of Asian Americans are uninsured (higher than the national average) and 12.5% live below the poverty line. Many also have language barriers which, along with the lack of financial resources, keep them from navigating America's convoluted healthcare system.

Studies also indicated that HBV infection has not received adequate attention from government and health care agents, healthcare providers, and the general public. For example, Asian-Americans comprise 12% New York City's population, however as of 2008, less than one percent of social services were channeled toward the Asian-American community.^{24,28-29}

CDC Recommendations for HBV Screening

Central Disease Control and Prevention (CDC) has increased its attention and efforts, and is implementing a more updated and strict guidelines and recommendations for HBV screening and vaccination over the years.³²⁻³³ Table 1 compares CDC guidelines published in 2005 and 2008 on HBV screening and vaccination.³²⁻³³

The highlight of the CDC's 2008 recommendations is to significantly expand HBV screening to all persons born in geographic regions with HBsAg prevalence of > 2%, compared to 8% recommended in 2005 guidelines. This will enhance the effectiveness of medical intervention on HBV screening. The updated guidelines also expanded 2005 guidelines to include new recommendations for public health evaluation and management for chronically infected persons and their contacts, men who have sex with men, immunocompromised individuals and injection-drug users.

Implementation of these recommendations will require expertise and resources to integrate HBsAg screening in prevention and care settings serving populations recommended for HBsAg testing. The updated guidelines also include information about management of patients with chronic hepatitis B. According to a press release by the CDC, recommended lab tests for people with chronic HBV infection should include a complete blood count and liver panel; tests for markers of HBV replication including hepatitis B e antigen (HBeAg), anti-HBe antibodies, and HBV DNA; and tests for coinfection with hepatitis C virus (HCV), hepatitis delta virus (HDV), HIV, and in some cases antibodies against hepatitis A virus (HAV).^{32,34-35}

The 2008 guidelines fail to satisfy all the agents and experts, though. Many believe more things have to be done. IOM,²² for example, convened a committee in 2008 to assess current prevention and control activities for HBV and HCV, and to determine ways to reduce new cases of HBV and HCV infections and illnesses and deaths from chronic viral hepatitis. The committee pointed out that surveillance information better prepares policy makers to allocate sufficient resources to viral hepatitis prevention and control programs, however surveillance data currently do not provide accurate estimates of the current burden of disease and are insufficient for program planning and evaluation, making current monitoring viral hepatitis in the U.S. challenging. Therefore the committee recommends that CDC conducts a comprehensive evaluation of the national hepatitis B and hepatitis C public health surveillance system to determine its current status. Further, CDC should develop specific agreements with all state and territorial health departments to support core surveillance for acute and chronic hepatitis B and hepatitis C, and conduct targeted active surveillance to monitor incidence and prevalence of hepatitis B and hepatitis C in populations not fully captured by core surveillance.

The CDC's Advisory Committee on Immunization Practices (ACIP), which provides recommendations on the control of vaccine-preventable diseases, recommended all infants and children and at-risk adults (people at risk for HBV infection from infected household contacts and sex partners, from exposure to infected blood or body fluids, and from travel to regions with high or intermediate levels of endemic HBV infection) should receive the hepatitis B vaccine. To prevent HBV transmission from mothers to their newborns, infants born to mothers who have hepatitis B should receive a first dose of the hepatitis B vaccine within 12 hours of birth.³⁶

ACIP also noted that first doses of the vaccine are often being missed or delayed, probably due to the lack of a delivery-room policy for HBV vaccination and that this substantially increases the risk of developing chronic hepatitis B. Therefore, the IOM committee recommends that all full-term infants born to women with hepatitis B receive the hepatitis B vaccine in the delivery room as soon as they are stable and washed.

ACIP recommends that all states mandate that the hepatitis B vaccine series be completed or in progress as a requirement for school attendance, since data has shown school-entry mandates increases HBV vaccination rates and reduce disparities in vaccination rates. Because only about half of at-risk adults have received the HBV vaccine, the committee recommends that additional federal and state resources be devoted to increasing hepatitis B vaccination in this population.^{33,37}

Clearly, the CDC 2008 recommendations for HBV screening and vaccination will have to integrate the suggestions from the public agents and experts, to meet all the needs of our commitments to fight against this important health problem.

Table 1. Comparison of between CDC Recommendations for HBV Screening between 2005 and 2008.

Suggest for screening	Recommendations in 2005	Recommendations in 2008
People from endemic areas	Individuals born in the areas with HBV prevalence $\geq 8\%$	Individuals born in the areas with HBV prevalence $\geq 2\%$ US born from the parents born in regions with HBV prevalence $> 8\%$
Pregnant women	yes	same
Infants born to HBsAg positive mothers	yes	same
Close contacts	Household contacts and sex partners of HBV-infected ones	same
High risk populations	All people with HIV; Persons who are the source of blood or body fluid exposures that might warrant post exposure prophylaxis (e.g., needle stick injury to a health-care worker or sexual assault)	Same and also added the following: Injection-drug users; Men who have sex with men (MSM) People who require immunosuppressive therapy (for example, cancer chemotherapy or drugs to prevent organ rejection after a transplant) Persons with unexplained abnormal liver function tests (elevated ALT and/or AST) Anyone else with a known HBV risk factor

Summary

HBV infection is a common disease in Asian Americans that can be complicated by cirrhosis and HCC. While the medical prevention and treatments of HBV infection have been dramatically improved, further improvement will be needed in guidelines for healthcare providers. A general inadequate awareness and many other barriers can negatively impact our commitments to screen, prevent, and treat HBV-related diseases. Further outreach and educational program to healthcare professionals, as well as risk population and general public, improvement of prevention and surveillance system, integration of hepatitis B service, and consolidation on the public health regulations are the eminent priority in the future.

Financial Disclosure

Dr. Xuejun Kong declares no financial interests related to this work.

Dr. Mark Li is the member of the speaker bureau of Bristol-Myers Squibb Company, Gilead Scientific Inc.

Dr. He-Qin Hu received educational grants from Bristol-Myers Squibb Company, Gilead Scientific Inc., Genentech Pharmaceuticals, Merck Corporation, and Vertex Pharmaceuticals. He is also the member of the speaker bureau of Bristol-Myers Squibb Company, Gilead Scientific Inc., Genentech Pharmaceuticals, and Merck Corporation.

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