

# HBV JOURNAL REVIEW

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## *Hepatitis B*

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### **Report Suggests 2.2 Million U.S. Residents Have Hepatitis B—Double the CDC Estimate**

What percentage of foreign-born residents in the United States have chronic hepatitis B? Many more than what the U.S. Centers for Disease Control and Prevention currently estimates, according to a study by Digestive Disease Institute researchers in Seattle.

The research team estimated the prevalence of hepatitis B virus (HBV) infection among foreign-born residents by first determining HBV infection rates in their countries of origin. They then applied those infection rates to the citizens who migrated to the United

States from those countries, as reported by the U.S. Census Bureau in 2009.

Researchers reviewed 256 surveys of immigrants from 52 countries (covering 689,078 persons) and 1,797 surveys of the general populations of 98 countries (covering 17.8 million people).

“We estimate a total of 1.32 million foreign-born people in the U.S. living with chronic hepatitis B in 2009,” they wrote in the November 2011 issue of *Hepatology*.

They estimated that 58% of those infected migrated from Asia and 11% migrated from Africa, where hepatitis B is highly endemic. About 7% migrated from Central America, a region with lower chronic hepatitis B rates but many more migrants

to the United States. “This analysis suggests that the number of foreign-born people living with chronic hepatitis B in the U.S. may be significantly greater than previously reported,” they wrote. “Assuming 300,000 to 600,000 U.S.-born persons with hepatitis B, the total prevalence of chronic hepatitis B in the U.S. (when foreign-born residents are added) may be as high as 2.2 million.”

The CDC currently estimates there are 800,000 to 1.4 million U.S. residents chronically infected with hepatitis B. However, CDC surveys often do not capture the infection status of new immigrants, homeless people, or people who have little contact with the nation’s health care system.

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## **Hepatitis B Patients Should Be Tested for Vitamin D**

Researchers at the 2011 Digestive Disease Week meeting reported that 64% of patients with hepatitis B or C infections have low levels of vitamin D, and doctors should start screening these patients regularly for the vitamin deficiency that can cause weakened bones and bone loss.

This deficiency in hepatitis B patients can be serious, considering that many patients are treated with antivirals that can also contribute to vitamin D deficiencies, according to researchers affiliated with the Weill Cornell Medical College in New York City.

The doctors reported that among 2,312 patients treated at their medical center between 2007 and 2009, only 17% had been tested for vitamin D levels. Of those who underwent vitamin D testing, 31% (122 of 395) were vitamin D insufficient and 33% (132 of 395) were vitamin D deficient. The prevalence of vitamin D insufficiency was similar among the 29% (115 of 395) of patients with chronic viral hepatitis

who had cirrhosis and those who did not. However, the difference in vitamin D deficiency among patients with cirrhosis and those without cirrhosis was significant (44% vs. 29%).

Interestingly, vitamin D insufficiency was more prevalent among those infected with hepatitis B than among those infected with the hepatitis C virus (HCV) (73% vs. 60%). There was not enough data to indicate if ethnicity of patients played a role in the vitamin D deficiency.

Past research has shown that low vitamin D levels tend to be more common in patients with advanced stage fibrosis and cirrhosis, but this study shows low levels of vitamin D can exist in patients who have chronic hepatitis B, but have not yet developed serious liver damage.

### **Experts Make the Case for Identifying Patients' HBV Genotypes**

Currently, doctors routinely screen hepatitis B patients for various antigens and antibodies, viral load, and alanine aminotransferase (ALT) levels (that can indicate liver dam-

age), but to date medical guidelines do not recommend screening patients in order to identify their HBV strain or genotype.

A British research team, writing in the November 2011 issue of *Current Gastroenterology Reports*, makes the case for screening patients for their genotype.

Genotype, they explain, influences the severity of liver disease as well as whether patients will respond to interferon treatment. Certain mutations in the virus also occur more frequently in patients with certain genotypes. Some of these mutations can increase a patient's risk of liver damage and cancer, which means these patients should be screened more frequently.

Genotypes A and B appear to have higher rates of hepatitis B "e" antigen (HBeAg) seroconversion (loss of HBeAg and development of "e" antibodies), while more advanced liver disease and liver cancer occurs more frequently with genotypes C and D. Meanwhile, genotypes A and B have better response rates to interferon treatment than genotypes C and D.

"Knowledge of HBV genotype enables clinicians to identify those patients at increased risk of disease progression while aiding the selection of appropriate antiviral therapy," they noted. "In conclusion, genotyping of chronic HBV infections can help practicing physicians identify those at risk of disease progression and determine optimal antiviral therapy."

### **Experts Suggest New Criteria for Deciding When to Stop Antivirals**

When can patients stop taking antivirals without risking a relapse? A group of Japanese researchers have come up with a possible answer.

They followed 126 hepatitis B patients who discontinued antivirals and identified which patients continued to have normal ALT levels (indicating no liver damage) and HBV DNA levels below 10,000 copies/mL (low viral load) after stopping treatment.

They found that at least 90% of patients with either detectable HBeAg or HBV DNA higher than 1,000 log copies/mL at the time of stopping antivirals

relapsed within one year.

They proposed that patients with nearly undetectable HBV DNA, HBeAg and hepatitis B surface antigen (HBsAg) levels may be able to safely stop treatment without risking a relapse. They also suggested that patients who had been taking antivirals for a prolonged period of time—in order to achieve undetectable HBV DNA and HBeAg—may experience lower relapse rates, according to the report in the November issue of the journal of *Hepatology Research*.

**Extended Interferon and Antiviral Treatment Needed to Clear Both HBeAg and HBsAg**

Researchers followed 38 HBeAg-positive patients—who lost both the “e” and surface antigens after they were treated with interferon alpha and an antiviral—for 12 months after treatment ended to see what treatments had the most success. They reported that lengthy periods of both interferon and antiviral treatments produced the most success.

Losing HBsAg is the goal of treatment among people chronically infected with HBV.

Those who cleared HBsAg were treated on average for 31 months. It took about 19.5 months for most patients to first lose HBeAg and develop “e” antibodies, and 25.5 months for them to lose HBsAg.

Researchers reported in the December issue of the *Journal of Gastroenterology and Hepatology* that 36 (95%) of the patients who lost HBsAg during treatment remained HBsAg-free 12 months after treatment ended.

**Potent Antivirals May Improve Liver Cancer Survival, or Prevent Its Recurrence**

An editorial in the *Journal of Gastroenterology and Hepatology* suggests that use of potent antivirals, such as tenofovir (Viread) or entecavir (Baraclude), may one day improve survival among people with liver cancer, or prevent its recurrence if tumors are surgically removed.

Those currently at highest risk of liver cancer are men over age 40, with cirrhosis

and a family history of liver cancer. However, the highest-risk group for cancer recurrence are patients who have been treated for liver cancer, but who continue to have detectable HBV DNA, even if their ALT levels are normal.

To date, there have been very few studies on the effectiveness of antivirals to suppress viral load and reduce the risk of liver cancer recurrence. However, the writer suggests that long-term use of more potent antivirals, such as tenofovir and entecavir, “is likely to increase the survival rate and probably will significantly reduce the (liver cancer) recurrence.”

“Hence, we await with interest the results long-term, large-scale prospective surveys of clinical outcomes involving these better antiviral regimens,” he added.

**Swift Treatment with Potent Antivirals May Save Patients Facing Liver Failure**

Some patients with chronic hepatitis B suffer sudden or acute liver damage or failure that can lead to death. A study published in

the November issue of the journal *Liver International* explores whether treatment with antivirals might prevent liver failure.

Recently, researchers have tried treating these patients with lamivudine (Epivir-HBV), which has increased survival to about 80%. But many of these patients were started on lamivudine belatedly, after they had developed severe liver damage.

“This suggests that prompt and timely antiviral therapy is crucial,” researchers noted. They promoted the use of stronger antivirals, such as tenofovir or entecavir when a sudden resurgence in viral load and liver damage is first diagnosed.

**Lower HBeAg Levels at Start of Entecavir Treatment Increases Chance of Success**

Researchers followed 95 HBeAg-positive patients treated with entecavir for 48 weeks to see which patients succeeded in achieving undetectable viral load.

According to their report published in the *Journal of Viral Hepatitis*, the patients who

had lower HBeAg levels when treatment began had the greatest chance at clearing the virus.

Researchers followed the patients' HBeAg and HBsAg levels every four weeks during the first 24 weeks of treatment and then every 12 weeks. They found HBeAg, HBV DNA, and HBsAg levels decreased most in patients who had HBeAg levels less than 360 PEIU/mL when treatment began.

Fifty-three patients (55.8%) attained undetectable viral load, and those who had steep declines in HBeAg at week 12 had higher chances at achieving undetectable viral load.

### **Researchers Find No Link between Hepatitis B and Breast Cancer**

Japanese researchers compared the incidence of breast cancer among women with no history of viral hepatitis infection and those with hepatitis B and/or hepatitis C infections.

They found hepatitis B did not increase a woman's risk of breast cancer, according to their report published in the November issue of the journal *BMC Cancer*. However, they found a small, increased

risk of breast cancer among women infected with the hepatitis C virus (HCV) who were under age 50.

### **Another Study Shows Doctors Missing Fibrosis in Patients with Normal ALTs**

Increasingly, researchers are finding that doctors are missing moderate to severe liver fibrosis in hepatitis B patients who have normal or slightly elevated ALT levels. ALT levels rise above normal when liver cells are damaged or die due to HBV infection.

Researchers at the Liver Center of Beth Israel Deaconess Medical Center (Harvard Medical School's teaching hospital), assessed blood test, ultrasound, and liver biopsy results from 140 hepatitis B patients.

According to a report published in the journal of *Hepatitis Research and Treatment*, 7 of the 56 HBeAg-positive patients who had normal ALTs and high viral load, actually had moderate to severe fibrosis and required treatment.

Among 84 HBeAg-negative patients, liver biopsies revealed that 10 patients with normal ALT levels actually had moderate-to-severe fi-

bro sis. Four of the 10 patients had moderate viral load, but six patients had been misdiagnosed as "inactive carriers" with undetectable HBV DNA levels and normal ALT levels.

HBeAg status, age, ethnicity, and long-term assessment of ALT levels and viral load, should be considered in patients with seemingly normal ALT levels, or levels at the upper end of normal range (20-40 IU/L), researchers suggested.

An unrelated study, presented at the annual Liver Meeting of the American Association for the Study of Liver Disease, reached a similar conclusion. Researchers performed liver biopsies on hepatitis B patients under age 40 also found higher-than-expected fibrosis among HBeAg-positive patients who had "normal" ALT levels. They found 13% of these patients had advanced fibrosis, which would have been missed by ultrasounds and blood tests.

### **Blood Test Can Identify Early-Stage Liver Cancer, in Time for Treatment**

A Chinese and U.S. research team have de-

veloped a blood test that is able to identify liver cancer through a blood sample, according to a report published in the November issue of the *Journal of Clinical Oncology*.

Currently, more than 60% of patients with liver cancer are diagnosed so late that there are no treatment options available. The researchers identified plasma microRNAs, which play a critical role in cell development and can serve as markers or indicators of certain tissue types. Recent research has shown that these microRNAs can be used to classify tumor cells—in this case HBV-related cancer cells.

Researchers compared three groups of people with hepatitis B (totaling 934) who were healthy, or had cirrhosis or liver cancer.

They identified a microRNA test that provided a high diagnostic accuracy of liver cancer. The test was also able to differentiate liver cancer samples from those from healthy or cirrhotic patients.

The test, the researchers wrote, was able to diagnose early stage liver cancer, and identify patients who would otherwise have mixed effective treatment.

