

HBV JOURNAL REVIEW

Volume 6, Issue 7

July 1, 2009

Hepatitis B

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Including Occult Hepatitis B Infection Raises HBV Infection Rate to 12.4% in South Africa

Increasingly, researchers are finding that many more people than expected have “occult” hepatitis B infection, characterized by no hepatitis B surface antigen (HBsAg), but discernable HBV DNA in the bloodstream.

A multinational research team, reporting in the July 2009 issue of the *International Journal of Infectious Diseases*, used highly sensitive tests to screen 502 South African patients for HBV DNA, the hepatitis B core antibody (anti-HBc) that indicates past infection,

and HBsAg.

They found 24 (4.8%) were HBsAg-positive, and 53 (10.6%) were positive for only anti-HBc. They then screened 43 of the 53 anti-HBc-positive people for HBV DNA and found 38 (88.4%) were positive and had occult HBV infection.

Previously, the average HBV infection rate among South Africans was estimated at 4.8%; however this study shows a chronic infection rate, including occult infection, to more accurately be at about 12.4%.

Researcher urged doctors to screen patients, including those also infected with HIV, for both HBsAg and HBV DNA in order to identify and treat patients with occult infection.

Active and Inactive HBV Carriers Risk Reactivation When Treated for Arthritis with TNFBA

Italian researchers report increased risk of hepatitis B reactivation in patients with active, occult, or resolved HBV infections who are treated with the rheumatoid arthritis drug tumor necrosis factor- α -blocking agents (TNFBA).

Reporting in the May 2009 issue of the *Journal of Rheumatology*, researchers reported that when treated with the anti-arthritic drug, HBsAg-inactive carriers who were pre-treated with the antiviral lamivudine (Epivir-HBV) had a lower risk of having detectable HBV-DNA or viral reactivation than those

HBV Journal Review

A publication of the Hepatitis C Support Project

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who had not been pre-treated with the antiviral.

TNFBA should be avoided in patients with active hepatitis B and should be used with caution in inactive HBsAg carriers, the researchers recommended. "In these patients, the risk of viral reactivation seems to be high, but it might be reduced by prophylactic lamivudine, which should probably be given for a long time when TNFBA is discontinued. Potential occult carriers might carry a low, but not negligible, risk of viral reactivation. They should therefore be monitored with particular care."

Fewer Than One-Third of Doctors Ask About or Vaccinate Adults at Risk of Hepatitis B

U.S. researchers surveyed 433 family physicians and 420 internists and found that only 31% of doctors routinely ask about risk factors for hepatitis B or recommend vaccinating adult patients who were at risk of hepatitis B.

Writing in the June

2009 issue of the *American Journal of Preventive Medicine*, researchers noted that fewer than 50% of adults with risk factors for hepatitis B infection have been vaccinated, and their survey showed neither patients nor doctors commonly inquired about the need for immunization.

Doctors' perceived barriers to hepatitis B vaccination included patients not disclosing high-risk behaviors, lack of adequate reimbursement for vaccination, and doctors' feelings of being too pressed for time to discuss risk factors. Most of the physicians surveyed were very (47%) or somewhat (38%) supportive of using standing orders (which authorize vaccinating patients without a physician's exam) for hepatitis B vaccination. However, limited staff time and patient reluctance to disclose sensitive information such as sexual practices or drug use to providers were perceived as barriers to using standing orders by many doctors.

The researchers noted the findings show that new strategies for vaccinating adults in primary care practices are needed.

Type 2 Diabetes Increases Liver Cancer Risk, Especially Among Men Treated with Insulin

Italian researchers monitored 465 liver cancer patients, 618 patients with cirrhosis, and 490 patients in a control group to identify any common risk factors among those who developed liver cancer.

According to their report published in the May 2009 issue of the *World Journal of Gastroenterology*, patients treated with the anti-diabetic drugs insulin or sulphonylureas were at increased risk of liver cancer.

They found diabetes mellitus was present in 31.2% of liver cancer patients, 23.3% of cirrhotic patients, and 12.7% of the control group. In 84.9% of liver cancer cases, type 2 diabetes mellitus was present before the cancer diagnosis. The risk of liver cancer was highest in patients treated with insulin or sulphonylureas, and lowest in diabetic patients treated with metformin.

"Our study confirms that type 2 diabetes

mellitus is an independent risk factor for liver cancer and pre-exists in the majority of liver cancer patients," they wrote. "Moreover, in male patients with type 2 diabetes mellitus, our data shows a direct association of liver cancer with insulin and sulphonylureas treatment."

HBeAg Negativity, Elevated AFP and Normal ALT Levels Indicate Increased Liver Cancer Risk

Researchers at the University of California in Los Angeles assessed the hepatitis B status among 128 cirrhotic patients, many of whom died during the five-year study.

Writing in the June 2009 issue of the journal of *Digestive Disease Sciences*, the researchers noted that 28 patients (21.9%) developed liver cancer during the study period and 36 (28.1%) died from non-liver cancer causes.

Those who developed liver cancer had elevated alpha fetoprotein levels (which indicates the presence of tumors), were HBeAg-negative, and had low

or normal alanine aminotransferase (ALT) levels. ALT levels increase when liver cells are damaged or die.

In contrast, those who died from non-cancer causes were HBeAg-positive, had low albumin and platelet counts, and elevated ALT levels.

HBeAg negativity, elevated AFP, and low ALT levels were strong predictors of liver cancer, researchers noted, while HBeAg positivity, abnormal liver tests, and low platelet counts were common among those who died from non-cancer causes.

Telbivudine-treated Patients Who Achieve Undetectable Viral Load at Week 24 Do Best

A multinational research team, participating in the GLOBE trial, followed 458 HBeAg-positive patients and 222 HBeAg-negative patients treated with telbivudine (Tyzeka) to determine which patients benefited most after two years of treatment with the antiviral.

According to their report in the July 2009

issue of the *Journal of Hepatology*, HBeAg-positive patients with moderate viral load and elevated ALT levels tended to do better on telbivudine. But by far, the patients who had achieved undetectable HBV DNA at week 24 of treatment achieved the best results.

- 89% of HBeAg-positive patients with moderate HBV DNA and slightly elevated ALT levels who reached undetectable HBV DNA at week 24 maintained undetectable viral load after two years; and 52% of them seroconverted and developed the “e” antibody. This group had a 1.8% telbivudine resistance rate.
- 91% of HBeAg-negative patients with moderate HBV DNA levels and undetectable viral load at week 24 sustained undetectable viral load over two years. The telbivudine resistance rate in this group was 2.3%.

“During telbivudine treatment, non-detectable serum HBV DNA at treatment week 24 is the strongest predictor for optimal outcomes at 2 years,” researchers wrote.

Hepatitis B Immunization Protection May Wane in HIV-Infected People

Experts at the 5th Annual Workshop on HIV and Hepatitis Co-infection in Lisbon, Portugal, heard several reports on the impact of hepatitis B infection on people infected with HIV. The following are some highlights:

- **Hepatitis B immunization may fail to protect the HIV-infected:** Experts presented cases where previously vaccinated people developed hepatitis B infections. In two cases, people developed chronic infections due to their HIV-weakened immune systems. One patient had had three full courses of vaccine, one before he acquired HIV, but failed to develop immunity. Three years after being diagnosed with HIV he developed acute hepatitis B. In the second case, the patient acquired hepatitis B in 2007 despite having been vaccinated and having previously developed immunity to hepatitis B. In a third case, a long-term survivor of HIV (diagnosed in the 1980s) was vaccinated for hepatitis B

in 2005 but presented with hepatitis symptoms in 2009.

- **Coinfected have faster declines in CD4 cells:** People coinfecting with HIV and HBV have considerably faster declines in infection-fighting CD4 cells than people infected with HIV and hepatitis C, or with just HIV alone, researchers reported.

- **Tenofovir highly effective:** About two-thirds of patients treated with tenofovir (Viread) and other antivirals develop undetectable HBV DNA levels. However, the 10% to 30% of patients who fail to respond are not always the same as those who fail HIV therapy, showing that transmitted drug resistance is becoming important in people with hepatitis B.

Increased death rates: Researchers found that among 3,500 HIV/HBV coinfecting patients, 10% developed liver cancer over 11 years. Researchers reported coinfecting patients had annual death rates from liver disease of 1.4%. In contrast, people infected with only HIV had an annual liver-related death rates of 0.17% and peo-

ple with only hepatitis B had a liver-related death rates of 0.08%.

HIV-HBV Patients Do Surprisingly Well After Liver Transplantation

People coinfecting with HBV and HIV often develop liver damage more rapidly than those with just HBV infection, but doctors have been hesitant to perform liver transplants on these patients due to the concurrent HIV infection. Researchers followed 13 HBV-HIV coinfecting patients who received liver transplants and then received antiviral therapy for one to five years to see how they fared.

According to their report published in the June 2009 issue of the journal *AIDS*, all patients survived during the study period and all had normal liver function and undetectable HBV DNA.

Researchers concluded that HBV-HIV coinfecting patients can successfully undergo liver transplantation with excellent results in terms of survival and control of HBV infection.

81% of U.S. Teens Have Up-to-Date Hepatitis B Vaccine Coverage

U.S. health officials conducted a nationwide immunization survey among 5,468 teens aged 13-17 and 2,882 doctors to assess hepatitis B vaccination coverage in this age group and found that 81.3% of the adolescents had up-to-date hepatitis B immunizations.

Older adolescents aged 15-17 years old had lower coverage (77.6%) than younger adolescents aged 13-14 (who had an 87.1% coverage rate). More than half of the 13-14-year-olds were vaccinated prior to age 3, while the 15-17-year-olds were vaccinated during their childhoods.

Younger teens who had private health insurance coverage and who had visited their doctors at age 11 or 12 had higher rates of immunization. Factors associated with up-to-date coverage among adolescents 15-17 years old included living in the Northeast, having a mother who was married, and having had a health care visit with a doctor at age 11 or 12,

according to the report published in the June 2009 issue of the *Journal of Adolescent Health*.

Hospital's Standing Orders to Screen Pregnant Women for HBV and Immunize Their Newborns Prevented New Infections

U.S. researchers, including those from the Centers for Disease Control and Prevention, studied why there was an unusually high number of perinatal (mother-to-newborn) HBV infections in one Arkansas county among babies born to mothers from the Marshall Islands, where HBV infection is prevalent.

Researchers studied records between 2003 to 2005 and compared how effectively all pregnant women treated at the hospital were screened for HBsAg, and whether their newborns were given the vaccine and HBIG to prevent transmission of infection to see if the Marshallese patients received substandard care.

Ten percent of 41 Marshallese births and 0.1% of 15 non-

Marshallese births were to HBsAg-positive women. Researchers found that Marshallese and non-Marshallese patients equally received the HBsAg screening, vaccine and HBIG within 12 hours of birth.

Because the hospital had standard orders to screen pregnant patients and immunize all infants, the intervention "likely provided a safety net to prevent perinatal HBV transmission in this high-risk population," researchers wrote in the May 2009 issue of the *Pediatric Infectious Disease Journal*.

Continued Antiviral Treatment Needed to Control HBV DNA after HBeAg Seroconversion

Researchers continue to investigate if and when it's safe to discontinue antiviral treatment after patients seroconvert (lose HBeAg and gain the "e" antibody).

Hong Kong researchers compared 22 patients who stopped lamivudine (Epivir-HBV) after HBeAg seroconversion to 79 patients who continued lamivudine after they

seroconverted.

Fourteen (64%) of those who discontinued treatment experienced a rebound of HBV DNA after 20 months, 82% had detectable HBV DNA after 4 years, and all eventually tested positive for HBV DNA.

There was no significant difference in the number of flares (spikes in alanine aminotransferase - ALT levels) between patients who had normal ALT levels and undetectable viral loads at the time they stopped lamivudine, compared to patients who had elevated ALT, detectable HBV DNA or both when they stopped treatment.

The rate of patients who regained HBeAg and experienced ALT flares five years after stopping treatment was 9% and 44% respectively.

In contrast, 62 (78%) of those who continued treatment maintained undetectable HBV DNA at the time of their last follow-up, whereas no patients had undetectable HBV DNA after stopping lamivudine, according to the report in the May 2009 issue of the *American Journal of Gastroenterology*.

Older Patients with Normal ALTs, or Those with Low, Fluctuating ALTs at Risk of Liver Damage

Researchers continue to investigate whether adults patients who have normal ALTs and high viral load should be treated or not. U.S. researchers performed two liver biopsies in 101 patients over a period of time to determine if there was undiagnosed liver damage occurring that should be treated.

They monitored Asian-American patients with normal or moderately fluctuating ALT levels (under 40 IU/L) and high HBV DNA levels who had never been treated.

The proportions of patients with normal ALT levels with significant fibrosis or liver scarring was 0% in those age 35 or younger, 22% in those aged 36-50, and 45% in those 50 and older. Among patients with fluctuating ALT levels, 22% of those under 35, 42% of those 36-50, and 69% of those 50 and older had significant fibrosis or liver scarring.

Researchers, writing

in the June 2009 issue of the *American Journal of Gastroenterology*, concluded that significant risk factors for liver damage in people with normal ALT levels included older age and fluctuating ALT levels.

Liver Cancer Risk Elevated in Women, Even after HBsAg Clearance

One of the few studies that focuses solely on women compared liver cancer rates in women with and without HBV chronic infection. Taiwanese researchers followed women over 17 years who were uninfected, had cleared HBsAg, or who were still chronically infected. They focused on 306 women in the group who developed liver cancer.

Liver cancer rates per 100,000 person years were 0.55 in HBsAg-negative women, 7.91 in HBsAg-positive and HBeAg-negative women, and 8.76 in HBsAg- and HBeAg-positive women.

Cancer rates per 100,000 person-years were 0.39 in uninfected women, 3.10 in chronic carriers who cleared HBsAg, and 9.01 in

persistent HBsAg carriers.

Surprisingly, cancer rates across the group were lower in women who had more children. They were 2.04, 1.55, and 1.66 per 100,000 person-years for women who had one, two, or three or more children, respectively.

Researchers, writing in the June 17, 2009, issue of the *Journal of the National Cancer Institute*, concluded that liver cancer risk was statistically significantly higher among women with chronic or active HBV infections and among those with persistent HBV infection or who had undergone HBsAg clearance.

