# Hepatitis B and C in African Americans: Current Status and Continued Challenges

Kimberly A. Forde,[*,‡] Orapin Tanapanpanit,[*] and K. Rajender Reddy[*]

*Division of Gastroenterology and Hepatology, Department of Medicine, and ‡Center for Clinical Epidemiology and Biostatistics, Department of Biostatistics and Epidemiology, Perelman School of Medicine, University of Pennsylvania, Philadelphia, Pennsylvania

**Viral hepatitis remains a public health concern in the United States, resulting in excess morbidity and mortality for the individual and representing a burden to societies as evidenced by billions of dollars in health care expenditures. As with many chronic diseases, race and ethnicity influence various aspects of disease pathogenesis, including mechanisms of persistence, disease progression, disease sequelae, and response to therapy. For hepatitis B and C infections, African Americans disproportionately bear a large burden of disease in the United States. The role and importance of African American race, however, have been less well-characterized in the literature among the population of viral hepatitis–infected individuals. The differences in epidemiology, manifestations of liver disease, response to therapy, and differential trends in liver transplantation in African Americans compared with other racial and ethnic groups deserve special attention. This review will address the current status of hepatitis B and C infection in African Americans in the United States and identify some of the remaining challenges in diagnosis, characterization of natural history, and treatment. For the purposes of this review, the terms *African American* and *black* will be used interchangeably throughout the text.**

*Keywords:* Hepatitis B; Hepatitis C; African American; Black; Disparities.

## Hepatitis B Infection

### *Epidemiology of Hepatitis B Infection*

Globally, more than 2 billion persons have evidence of hepatitis B virus (HBV) infection, and nearly 200–375 million of those have serologic evidence of chronic infection.[1] Although prior estimates of HBV infection in the United States have ranged from 800,000 to 1.4 million, emerging data suggest that this is an underestimate of disease burden, with infection in 2.2 million persons being proposed and of which immigrants bear the heaviest burden.[1–3] Furthermore, an estimated 1.4 million HBV-infected individuals are unaware of their infectious status, and important opportunities for treatment of chronic infection and surveillance for hepatocellular carcinoma (HCC) are being missed.[4]

In the United States, an estimated 35,000 new diagnoses of acute HBV infection were established in 2010.[5] This represents a decline of nearly 80% when compared with the rate of new HBV infections in the early 1990s before implementation of HBV vaccination programs. When examining incidence rates stratified by race and ethnicity, African Americans have the highest incidence of acute HBV infection, with 1.7 cases per 100,000 persons reported in 2010. This is in contrast to a rate of 0.6 per 100,000 persons in Asian Pacific Islanders and Hispanics, groups in the United States with the lowest HBV incidence.[5] The incidence rate of acute HBV infection for blacks has consistently been higher than that of other racial and ethnic groups since 2000.

Data from the National Health and Nutrition Examination Survey (NHANES) II and III suggest that the age-adjusted prevalence of chronic infection or serologic markers of past exposure to HBV in blacks was 5.5% and 4.9%, respectively; these rates failed to change during the years of study.[6] In this group, rates of chronic infection ranged from 0.33% to 0.42%. In addition to identifying foreign-born status as a risk factor for increased HBV prevalence, as defined by hepatitis B surface antigen (HBsAg) or hepatitis B core positivity, African American race was associated with an age-adjusted prevalence of 15.8% for 1976–1980 and 11.9% for 1988–1994. Furthermore, being black was associated with a 3.9-fold increase in odds of HBV positivity in comparison to whites.[6] Additional analyses in NHANES data found that differences in HBV prevalence rates between African Americans and other groups persisted after adjustment for important risk factors including demographic, socioeconomic, and behavioral characteristics.[7] These data suggest that factors other than socioeconomics and other risk factors account for

*Abbreviations used in this paper:* HBeAg, hepatitis B e antigen; HBsAg, hepatitis B surface antigen; HBV, hepatitis B virus; HCC, hepatocellular carcinoma; HCV, hepatitis C virus; IFN, interferon; IL, interleukin; MELD, Model for End-Stage Liver Disease; NHANES, National Health and Nutrition Examination Survey; PEG-IFN, peginterferon; RBV, ribavirin; SNP, single nucleotide polymorphism; SVR, sustained virologic response.


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an increased prevalence of HBV infection in African Americans.

### Natural History of Hepatitis B Infection

The natural history of hepatitis B infection, including its incubation period, symptomatology, and chronicity, has been well described.[8] No studies to date have examined differences in the natural history of HBV in African Americans or made comparisons to other racial and ethnic groups.

Chronic HBV infection may be asymptomatic or result in a range of manifestations of liver disease including chronic hepatitis, cirrhosis, or HCC. With regard to HCC, African Americans assume a greater burden of disease, with a notable increase in both HCC incidence and HCC-related mortality when compared with whites.[9,10] Yu et al[11] compared HCC risk factors in African Americans and whites. They found that African Americans had higher rates of viral hepatitis, coinfection with HBV and hepatitis C virus (HCV), and metabolic risk factors such as diabetes mellitus that increased their risk of HCC. In addition, because of the high prevalence of genotype A HBV infection in blacks, a genotype associated with a 4-fold to 5-fold increase in risk of HCC in black Africans,[12] African Americans may have risk factors for HCC that result in a markedly elevated and additive risk of HCC. Unfortunately, comparison data were not available for other racial groups such as Asians and Hispanics in the above study. Clearly, more research is required to further elucidate these aspects of HCC risk in African American patients with chronic HBV infection.

Because of the high risk of HCC in the context of viral hepatitides for many patient populations, surveillance for HCC is now recommended in select groups.[13] One such group, sub-Saharan Africans, tend to have not only a high incidence of HCC but also a high incidence of HCC at a younger age.[14] In a cohort of Africans with HCC, HBV serologies including HBsAg and hepatitis B e antigen (HBeAg) were more prevalent in patients younger than 30 years of age.[15] Although there are several studies of Africans that have examined their risk of HCC and demonstrated the importance of HCC surveillance in this group, such data are not available for blacks from other regions including the United States.[15–17] However, because of the increase in HBV infection in African Americans and their higher risk of HCC, it may be prudent to extend surveillance recommendations to this high-risk population.

### Viral Genotype and Host Genetic Diversity in Hepatitis B Infection

**Hepatitis B virus genotypic variability.** HBV genotype is an important determinant of disease progression with a notable influence on disease severity and response to HBV-directed therapy.[18–23] A review of HBV genotypes suggested that there are differences in HBV genotype distribution by race and ethnicity and place of birth. With respect to African Americans, 84% were infected with genotype A, followed by genotypes C and D at 6% and 4%, respectively.[19] In whites, genotypes A and D were most prevalent, as seen in 71% and 21% of the cohort, respectively. In comparison, genotypes B and C were observed most frequently in Asians. In the study, genotypes A and C were associated with HBeAg-status, and non–genotype B infection was an independent risk factor for abnormal alanine aminotransferase levels and decompensated cirrhosis. Although data are limited, it can be gleaned that there may be differences in disease progression that are mediated by differences in viral genotype distribution.

**Host genetic diversity.** Interleukin (IL)-10 promoter polymorphisms have been associated with HBV infectious outcomes, including spontaneous HBV clearance, HBeAg seroconversion, development of chronic liver disease, and incidence of HCC.[24,25] In addition, foci near the IL-19 and IL-20 genes have been associated with regulation of proinflammatory cytokine production early in viral infections. To further explore racial differences in response to acute HBV infection, Truelove et al[26] examined the effect of single nucleotide polymorphisms (SNPs) in the IL-10, IL-19, and IL-20 genes in African Americans and whites in a nested case-control study. It was found that African Americans who were heterozygotes at the rs1518108 locus of IL-20 were more susceptible to chronic HBV infection. This locus is also of importance in the genetics of host response in HCV infection.[27] Furthermore, polymorphisms in the IL-10 promoter region were observed to be an important determinant of HBV infection. In African Americans, SNP variants at the IL-10 and IL-20 loci determined the establishment of HBV infection, whereas in those of European ancestry, IL-20 variants solely influenced recovery. Although more work needs to be done to clarify the genetic and immunologic basis of the development of HBV infection stratified by race, differences in host genetics may contribute to the racial and ethnic differences observed in HBV prevalence.

### Treatment and Outcomes in Chronic Hepatitis B Infection

There is a relative scarcity of data regarding treatment outcomes for chronic HBV infection in African Americans undergoing interferon (IFN) and/or nucleoside/nucleotide-based antiviral therapy. A long-term follow-up study of patients who had undergone therapy with IFN observed that African American patients were much more likely to respond to therapy.[28] Of note, all African American responders not only cleared HBeAg and HBV DNA from the serum, but all cleared HBsAg, a relatively rare milestone with HBV therapy that occurs in up to 7.8% of patients on therapy.[29] Unfortunately, there were few African Americans who