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Ethnic Disparities in Chronic Hepatitis B Infection: African Americans and Hispanic Americans

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Abstract

Chronic infection with hepatitis B affects more than 240 million persons worldwide and is a major public health concern. Despite national and global initiatives to promote hepatitis B elimination, including newborn vaccination, catch up vaccination in adolescents and high-risk adults, screening of the blood supply and treatment of those in need, both new infections and a reservoir of chronic infections continue to result in morbidity and mortality. As with many chronic diseases, racial and ethnic disparities are seen in hepatitis B virus infection.

Purpose of Review—The goal of this review is to synthesize the data concerning the burden of hepatitis B infection in African Americans and Hispanics, two racial/ethnic groups in the United States who encounter barriers in access to care, low engagement in care and low utilization of diagnostic and treatment services.

Recent Findings—Recent data, though sparse in certain areas, continue to suggest differences in rates of incidence and prevalence of hepatitis B virus infection in African Americans, and differences in screening, specialty referral and initiation of therapy for African Americans and Hispanics. Data are lacking about differences in liver disease progression and manifestations in both African Americans and Hispanics.

Summary—Disparities in hepatitis B diagnosis, disease management, treatment and prevention remain for African Americans and Hispanics. These disparities require a commitment from governmental and public health organizations. The efforts should include increasing vaccination in those most susceptible to infection, screening those at highest risk for infection, initiating antiviral therapy in those who require it and monitoring for liver-related complications, such as decompensated cirrhosis and hepatocellular carcinoma in the chronically infected. This multi-pronged approach is necessary to realize hepatitis B elimination.

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Compliance with Ethical Guidelines

Conflict of Interest

Kimberly A. Forde declares no potential conflicts of interest.

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Keywords

African Americans; Chronic Infection; Disparities; Hepatitis B; Hispanics

Introduction

Worldwide, chronic infection with hepatitis B virus affects approximately 240 million persons [1]. More than 668,000 people die annually across the globe from the complications of chronic hepatitis B infection, which include chronic liver disease, cirrhosis, decompensated liver disease and hepatocellular carcinoma (HCC), all of which may occur in the absence of overt symptoms [2]. Chronic hepatitis B infection, the most prevalent blood-borne infection globally, is of highest prevalence in sub-Saharan Africa and East Asia, affecting up to 10% of these respective populations [1]. In highly endemic areas, hepatitis B is primarily spread through vertical transmission, from mother to child, though horizontal transmission (contact with infected blood or body fluids in the uninfected/unvaccinated host) also plays a role [1]. While global vaccination efforts have reduced the rate of chronic infections in low, medium and high endemic regions, and hepatitis B directed antiviral therapy can prevent the development of hepatitis B liver complications, such as decompensated cirrhosis and HCC, access to diagnostic services and antiviral treatment in resource-poor settings is limited, and adherence to suggested diagnostic and treatment strategies in resource rich settings is modest. Chronic hepatitis B infection therefore remains a public health burden throughout the world.

In 2016, the World Health Organization implemented the Global Health Sector Strategy on Viral Hepatitis, a strategy outlining the organization's efforts towards realizing hepatitis B elimination [3]. This roadmap towards hepatitis B elimination outlines a strategy to achieve a 90% reduction in new hepatitis B virus infections and 65% reduction in hepatitis B-related death by 2030 [4]. In this document, a strategy for elimination of chronic hepatitis B is presented with consideration of the current burden, proposed strategies for elimination, identification of achievable goals, identification of action items, and recognition of important considerations for implementation.

In the United States (US), approximately 850,000 – 2 million people have hepatitis B, with a large burden of disease observed in immigrants and racial/ethnic minorities [5–8]. This review will focus on the areas of interest as emphasized by the Global Health Sector Strategy on Viral Hepatitis. In addition, it will highlight the US strategy as stated in the Institute of Medicine report published in March of 2017 as it pertains to Blacks or African Americans (hereafter referred to as African Americans) and Hispanic and Latino American populations (hereafter referred to as Hispanics) [3, 9]. Barriers in access to care, low engagement in care and low utilization of diagnostic and treatment services have historically disadvantaged these two racial/ethnic groups. These factors may also lead to disparities in movement through the hepatitis B continuum of care in these 2 patient groups [3].

Towards Eliminating Viral Hepatitis

Burden of Disease

In the US, data from the National Health and Nutrition Examination Survey (NHANES), a sample of the civilian non-institutionalized population, from years 1988–2012 suggest that hepatitis B exposure and subsequent chronic infection have declined over time (5.5%, 4.8% versus 3.7% of population exposed and 0.4%, 0.3% versus 0.3% for those persons with serologic evidence of chronic infection for years 1988–1994, 1999–2006 and 2007–2012, respectively) [8]. The dramatic decline in hepatitis B infection has been realized as a result of a multipronged national effort to curtail infection, including universal vaccination of newborns and catch-up vaccinations for children and adolescents, implemented in 1991, screening of pregnant women, in practice since 1984, and screening of the US blood supply, initiated in 1972 [10–12]. Despite these efforts, minorities remain at high risk for hepatitis B infection.

African Americans

Incidence and Prevalence, Table 1: Regarding new hepatitis B infections, the rate of acute infections has declined by greater than 63%, with just over 8,000 cases reported in year 2000 and just under 3,000 cases reported in year 2014 [13]. From 2009–2014, the number of new hepatitis B cases has been relatively stable. Though there has been a decline in infection rates for all racial and ethnic groups from 2000–2014, African Americans continue to have the highest rate of new infections [13]. New infections among African Americans were most often reported in patients who were male, 30–39 years of age, and those who engaged in high-risk behaviors that increase risk of transmission of hepatitis B infection, particularly use of intravenous (IV) drugs, men who have sex with men (MSM), and having two or more sexual partners [13].

In the second and third iterations of NHANES, African Americans had the highest prevalence of chronic hepatitis B infection (age-adjusted prevalence 15.8% and 11.9%, respectively in NHANES II and III) [14]. In data spanning 1999–2008, African American men had the second highest prevalence of chronic infection (0.73% overall) as well as the second highest prevalence of hepatitis B exposure (10.4% overall). This rate was only surpassed by those persons who reported their race/ethnicity as other, including Asian and foreign-born persons who are known to bear the largest burden of hepatitis B in the US [6]. In this study, African Americans represented 26% and 31% of patients exposed to and with chronic hepatitis B infection though they only represent 12% of the general population, speaking directly to the burden of hepatitis B infection in this patient population [6]. In the most recent review of the NHANES data, African Americans again were found to have a 2–3 fold higher prevalence of chronic hepatitis B infection compared to the general population [8].

The explanation for the high incidence of hepatitis B and prevalence of chronic infection among African Americans remains poorly understood. However, it has been proposed that high rates of exposure and low rates of immunization in those with high-risk behaviors may be of importance [15]. Though little data exists on the number of IV drug users who are

vaccinated against hepatitis B, one small study suggested that approximately 10% had immunity and a staggering 37% had evidence of active infection [16]. Additionally, in this high-risk population, African American race was associated with higher rates of infection, supporting low rates of vaccination in highly susceptible hosts. Similar disparities in patterns of chronic infection and hepatitis B immunity have been seen in other high-risk populations, including MSM and those who are incarcerated. This last group are a particularly vulnerable population for whom screening, vaccination of those susceptible and treatment of chronic infection is, for the most part, not provided. Additionally, incarceration rates disproportionately affect men of color [17]. In a study of men with a history of incarceration, 46% of participants were African American and 55% were susceptible to hepatitis B, speaking directly to the skewed racial composition of those incarcerated and need for implementation of vaccine programs in correctional facilities [18, 19].

Chronic Disease/Disease Manifestations: Though few data are published on racial differences in seroconversion after exposure to the hepatitis B virus, there are data suggesting that differences in single nucleotide polymorphisms (SNPs) may influence liver disease outcome. African Americans with SNPs in the interleukin (IL)-10 or IL-20 coding regions were found to have certain genotypes that were associated with spontaneous recovery and others being associated development of chronic infection [20].

IL-28B, a genetic polymorphism associated with spontaneous clearance of and interferon treatment responsiveness in chronic hepatitis C infection, has also been implicated in certain racial groups as being of importance to hepatitis B viral load levels and severity of hepatic inflammation [21–24]. However, to our knowledge such studies have not been conducted in populations that include African Americans.

In a recent study from a Veteran's Administration (VA) cohort, African American race was associated with an increased risk of development of HCC in the setting of chronic hepatitis B without concomitant cirrhosis [25]. It is unclear why this increase in HCC risk was noted in African Americans, a finding the authors suggest could be on the basis of host genetics, early acquisition of infection, or other comorbid or environmental exposures which increase the risk. Regardless, the near 7-fold increase in risk of HCC in African Americans highlights the need for appropriate implementation of HCC surveillance programs. In this study, only 31% all participants who had HCC but no cirrhosis were enrolled in an HCC surveillance program [25].

Treatment: Data from the Racial and Ethnic Approaches to Community Health across the US (REACH US) study suggest that there are disparities with respect to hepatitis B screening (discussed below), referral to care, and initiation of antiviral therapy [26]. In this study, among the 1235 persons reporting a history of chronic hepatitis B infection, only 33% reported being seen by a physician. Additionally, of those African Americans with chronic hepatitis B infection engaged in care, only 51.3% had ever been administered antiviral treatment for their infection. This is the lowest percentage of all racial and ethnic groups evaluated in the study, though antiviral therapy is just as efficacious and safe in African Americans as in other hepatitis B infected populations [26, 27].

Liver transplantation is a treatment modality that may be employed for chronic hepatitis B-related decompensated cirrhosis or for the treatment of hepatitis B-associated HCC. Racial disparities have been demonstrated in both utilization of liver transplantation and in the post-transplant outcomes. In the setting of hepatitis B infection specifically, the data are conflicting at best. A study from 2009, including 274 patients, suggested comparable post-transplant outcomes for African Americans when compared to other racial groups [28]. A more contemporary study of 738 patients from 10 academic centers, suggested that African Americans had higher rates of mortality, a finding for which the reasoning remains unclear [29].

Hispanics

Incidence and Prevalence, Table 1: In the year 2014, Hispanics had one of the lowest rates of acute hepatitis B infection, 0.29 cases per 100,000 persons in the population [13]. Mirroring the rates of acute infections, data from NHANES from 1999–2008 also suggest a low prevalence of exposure to and chronic infection with hepatitis B among Hispanics. Persons of Hispanic ethnicity had the lowest prevalence of hepatitis B in the NHANES study, 0.05%, a prevalence that was even lower than that for non-Hispanic whites in the study (0.11%) [6]. The prevalence was notably low for Hispanics born in the US or Mexico (0.026%) but was higher for Hispanics born outside of the US (0.59%), suggesting that hepatitis B prevalence is likely in the intermediate range if US and foreign born Hispanics were to be evaluated as one group. In the sample, approximately 3.5% of Hispanics had been previously exposed.

Chronic Disease/Disease Manifestations: Hispanics constituted approximately 16 percent of the US population in 2010 and represent the largest and fastest growing racial/ethnic group in this country [30]. Though it is expected that Hispanics will represent close to 22.8% of the US population by 2035, little is known about rates of development of chronic hepatitis B virus infection, the course of chronic infection in this subgroup, and differences in disease manifestations in Hispanic patients exposed to or chronically infected with hepatitis B [31]. Unfortunately, Hispanics have higher rates of death from chronic liver disease and cirrhosis when compared with whites, a rate that was double that seen in the comparator group [31]. Additionally, in the Multiethnic Cohort Study, an on-going population based cohort study in over 200,000 men and women in Hawaii and California, though non-alcoholic fatty liver disease (NAFLD) was the most prevalent form of liver disease noted in Hispanics, approximately 3% of cases in Hispanics were secondary to chronic hepatitis B, a percentage comparable to other racial and ethnic groups [32]. Furthermore, work performed in this diverse cohort suggests that Hispanics also have the highest rates of HCC incidence [33]. Clearly, more work needs to be done to define differences in hepatitis B disease progression in Hispanics infected with hepatitis B.

Treatment: To date, there are few data available on the likelihood of being initiated on antiviral therapy for hepatitis B infection and how or if initiation of therapy differs based on race and ethnicity. In REACH US, 34% of Hispanics diagnosed with hepatitis B infection reported being seen by a physician and of those 66.7% had ever been initiated on hepatitis B-directed antiviral therapy [26]. Furthermore, no studies have determined the relative

efficacy and/or adverse events associated with therapy in those patients of Hispanic ethnicity. Regarding liver transplantation and its utility for the treatment of chronic liver disease and/or HCC, in Hispanics, historical data suggest that outcomes of liver transplantation for chronic hepatitis B yielded favorable results in this patient population, with greater than 70% of patients surviving to greater than 2 years post transplant [34].

Strategies for Hepatitis B Elimination among African Americans and Hispanics

Newborn Vaccination/Catch up Vaccination in Adolescents, Adults, and High-Risk Groups

African Americans—Though there are disparities in acquisition of new hepatitis B infections and establishment of chronic infection with hepatitis B in African Americans, rates of hepatitis B immunity, as evidenced by presence of antibody to hepatitis B surface antigen (anti-HBs) in the serum, were found to be high in children 2–6 years of age (68.6% – 52.1%) and varied little based on race, ethnicity or socioeconomic status [6]. These rates of vaccination, though favorable, were less than those expected based on estimates of the number of children receiving the 3 dose vaccination schedule from 2004–2009 (> 90%) [35, 36]. However, these estimates may reflect real world uptake of the Advisory Committee on Immunization Practices (ACIP) guidelines of the Centers for Disease Control and Prevention (CDC) as well as waning of anti-HBs in the serum, a process that is noted to occur in up to 40% of hepatitis B vaccinated subjects but does not necessarily result in a waning of immunity to hepatitis B infection [10, 37–40].

Regarding vaccination of adults and those at high risk for infection, rates of vaccination did, in fact, vary by race and ethnicity. Estimates from the CDC for 2014 suggest that fewer African Americans underwent hepatitis B vaccination than did whites (29.9% versus 36.3%, $p < 0.001$). Furthermore, in prior evaluations of rates of vaccine coverage in the United States, African Americans at highest risk for hepatitis B infection, including those that had HIV coinfection, a history of other sexually transmitted infections (STIs), were MSM, and had a history of injection drugs, were found to have low rates of vaccine coverage. These rates approached 42% in those African Americans at high risk compared to 44.5% in whites and 33.6% versus 34.9% for those patients at average risk [41].

Hispanics—Vaccine coverage in US Hispanic patients follows similar trends to that seen in African Americans. NHANES data from 1999 through 2008 suggest no significant difference in vaccine coverage for children 2–6 years of age based on ethnicity [6]. However, differences in rates of adult vaccine coverage have existed for years. In the 2010 evaluation of vaccine coverage published by the CDC, adult Hispanics had the lowest rates of hepatitis B vaccine coverage, regardless of the presence or absence of a history of high-risk behaviors (33.8% versus 44.5% compared to whites with a history of high-risk behaviors in 19–49 year olds; 24.7% versus 33.1% in 19–49 year olds with no reported history of high risk behaviors) [41]. Unfortunately, this disparity in vaccine coverage rates has persisted, with the most recent evaluation of coverage in the US in 2014 also suggesting that Hispanics have the lowest rates of vaccination coverage [42].

The disparate rates of vaccination coverage for racial and ethnic minorities speak to the need for targeted efforts for catch up hepatitis B vaccinations for adults, particularly those at high risk for hepatitis B exposure. Of course, as resources are limited for vaccination efforts across the board, the goal must be to strike a balance between childhood immunization and adult vaccination [43]. However, a directed approach, targeting those high-risk patients who present to STI clinics or in those incarcerated for the short or long-term may be an optimal approach, with some studies suggesting that the rate of hepatitis B infection could be reduced by up to 50% with implementation of vaccination of susceptible hosts in these settings [18, 43].

Hepatitis B Screening Programs

African Americans—Clear disparities have been noted in hepatitis B screening rates, rates that are lower than suggested even in high-risk groups. In REACH US, of the 53,896 minority respondents in the study, 39.2% reported ever being tested for hepatitis B. For African Americans, this translated into approximately 40% ever being tested. Additionally, hepatitis B screening declined with age, with only 10% of those 55–64 years being offered screening, a phenomenon seen in all racial and ethnic groups [26]. Low rates of screening have also been demonstrated in high-risk groups. In a study from Kaiser Permanente Southern California spanning years 2008–2011, only 28% of patients with STIs were tested for hepatitis B, though testing improved over the period of the study. However, the odds of being tested were inversely associated with African American race, suggesting a missed screening opportunity in this population [44].

Hispanics—In REACH US, Hispanics were less likely to be tested for hepatitis B than any other racial/ethnic group in the study (35.6%) [26]. Unfortunately, data are sparse with respect to screening rates for Hispanics with high-risk behaviors.

Specialty Referral and Treatment Initiation

In REACH US, of the 1,235 participants who reported a history of being diagnosed with chronic hepatitis B infection, one third reported being seen by a physician at the time of survey. Of those, 51% of African Americans and 66.7% of Hispanics had ever taken medication for hepatitis B [26]. Unfortunately, the data available for review could not determine which of these patients met established clinical indications for the initiation of therapy. In a study conducted in a VA cohort of patients with chronic hepatitis B infection, approximately 40% of patients moved through the hepatitis B continuum of care to the receipt of antiviral therapy. It is not clear however if there were racial/ethnic disparities in movement through the continuum [45].

Goals and Targets

In addition to guidance provided by the WHO, the Institute of Medicine, and Healthy People 2020, the US government's agenda for developing a healthier nation have outlined several goals as they pertain to the eradication of hepatitis B infection [3, 9, 46, 47]. In the report issued by the Institute of Medicine, titled "A National Strategy for the Elimination of Hepatitis B and C", several goals required for the elimination of chronic hepatitis B were

explicitly stated. These included ending transmission (perinatal, childhood and adults) and reducing morbidity and mortality from ongoing infection (slowing progression and reducing deaths) [9]. Many of the specific topic areas for hepatitis B infection as stated in the Institute of Medicine report and Healthy People 2020 are of importance to addressing hepatitis B infection in racial and ethnic minorities (Table 2).

The achievement of these goals will directly reduce transmission of hepatitis B infection to those susceptible and address the disease and healthcare disparities discussed above.

Identifying Action Items

The following action items are of direct importance to increasing vaccination, testing and treatment of hepatitis B infection in African Americans and Hispanics:

Education of Patients and Providers—Gaps in the knowledge of patients, stigma associated with viral hepatitis, and lack of knowledge of hepatitis B screening criteria and treatment guidelines on the part of providers serve as barriers to the delivery of hepatitis B care. In the BfreeNYC program, a successful New York city pilot program charged with increasing screening for and treatment of hepatitis B in immigrants populations, information was provided to potential patients in their native language and in a culturally sensitive fashion, including by the creation of radio segments, conducting educational workshops and posting education on a centralized study website [48]. This strategy was highly effective in engaging the target community and in decreasing the stigma associated with the disease process. With respect to providers, customized templates for history taking and lab order bundles were used to simplify the care provision process for primary care providers who managed many of these patients in their offices without the need for referral to specialists, a type of care model demonstrated in the treatment of chronic hepatitis C infection [49]. These approaches helped to make BfreeNYC one of the most successful hepatitis B screening and treatment programs, providing services to approximately 9000 participants.

Structured Approach to the Delivery of Vaccination (High-Risk), Screening and Harm Reduction Services—Implementation of structured vaccination, screening and harm reduction programs, with a focus on providing resources to STI clinics and prisons, will assist in delivery of vaccination to those at highest risk for new hepatitis B infections.

Partnerships for the Provision of Treatment Services—The BfreeNYC program successfully provided for the medical needs of those study participants who did not have medical insurance to pay for hepatitis B diagnostic and treatment services [48]. Use of non-specialized providers with additional training in the treatment of chronic hepatitis B infection and federally qualified health centers may be able to assist with the treatment of uninsured or underinsured persons with chronic hepatitis B infection, a population likely to be large given the burden of infection in immigrants and racial/ethnic minorities.

Financial Infrastructure—Though the BfreeNYC program ran from 2004 through 2008 and provided care to just fewer than 9000 participants, the cost of the program was estimated at 8 million dollars. Additionally, though screening and vaccination costs were relatively

inexpensive (\$273/person), the cost of identifying a person with chronic hepatitis B infection (\$2243) and annual costs associated with testing and antiviral treatment (\$1598) constituted 40% of study expenditures [48]. Hence, elimination of chronic hepatitis B infection is an expensive undertaking, with the best and least expensive approach being prevention of infection.

Key Considerations for Implementation

Even a hepatitis B elimination strategy dependent on vaccination will require coverage of the vaccine for those who are underinsured or uninsured. Future hepatitis B elimination plans in the US should address the need for vaccination of not only newborns but also those who require catch-up vaccination and those engaging in the most high-risk behaviors. Additionally, screening for and treatment of those with chronic infection will require health care coverage to be most impactful. The burden of such a strategy to eliminate hepatitis B virus infection in the US can only be realized through the conduct of more research in special populations, including racial and ethnic minorities (Table 3) and widespread implementation efforts based on up to date evidence about disease burden and focus on areas of greatest need.

Conclusion

In conclusion, hepatitis B remains a public health burden and for many populations, including immigrants and racial/ethnic minorities, is a leading cause of morbidity and mortality. In racial and ethnic minorities, hepatitis B eradication can be realized by continuing national vaccination efforts for infants and children, increasing vaccination coverage in those at highest risk for infection, providing culturally appropriate education about infection, and providing affordable vaccination, testing and treatment services. Implementation of these strategies will ensure that hepatitis B remains a preventable disease, one that is eliminated in the US.

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Table 1

Comparison of Epidemiology, Screening Rates, and Chronic Disease Management of Hepatitis B Infection in Whites, African Americans, and Hispanics

Characteristic	White Americans	African Americans	Hispanic Americans
<i>Epidemiology</i>			
Incidence (cases/100,000)	0.86	0.88	0.29
Prevalence (%) ^{&}	0.10	0.6	0.06
Vaccine Coverage (%) [^]	25.2	25.0	20.2
Mortality Rates (deaths/100,000) [*]	0.32	0.80	0.38
<i>Screening Rates</i>			
Proportion Tested (%)	<i>a</i>	40.4	35.6
<i>Chronic Disease Management</i>			
Physician Referral (%)	<i>a</i>	24.0	34.3
Treatment (%) [§]	<i>a</i>	51.7	66.3

[&] Adjusted prevalence of chronic hepatitis B virus infection; NHANES 2007–2012.

[^] Age specific prevalence of hepatitis B virus vaccine immunity (anti-Hepatitis B surface antigen); NHANES 2007–2012.

^{*} Rates are age-adjusted per 100,000 U.S. standard population in 2000.

^a Point estimates not obtained in study referenced.

[§] Percentage reflects number of patients treated out of those in care at the time of data collection.

Table 2

Healthy People 2020: Objectives for Hepatitis B Eradication

Broad Objective	Specific Objective	Goal
Reduce, eliminate, or maintain cases of vaccine-preventable diseases	Reduce new cases among persons aged 2 – 18 years	0 cases
Increase vaccine coverage among high-risk populations	Increase vaccine coverage among injection drug users	NA
	Increase vaccine coverage among MSM	
Reduce hepatitis B	Reduce new infections in adults aged 19 years and older	1.5 cases/100,000
	Reduce new infections in injection drug users	215 cases
	Reduce new infections in MSM	45 cases
Testing/Awareness	Increase proportion tested for hepatitis B virus within minority communities experiencing health disparities	NA

Table 3

Research Needs

Area of Focus	African Americans	Hispanic Americans
<i>Epidemiology</i>	Determine incidence and prevalence in high-risk populations *	Determine incidence and prevalence in high-risk populations * Determine incidence and prevalence in immigrants from different Latin American countries to better target screening efforts
<i>Prevention</i>	Identify barriers to receipt of vaccination	Identify barriers to receipt of vaccination
<i>Chronic Disease Management</i>	Define natural history of chronic infection Determine differences in linkage to care/treatment initiation in large cohorts Explore models of health care delivery that maximize engagement in care/disease treatment	Define natural history of chronic infection Determine differences in linkage to care/treatment initiation in large cohorts Explore models of health care delivery that maximize engagement in care/disease treatment

* High-risk populations include those incarcerated, men who have sex with men and intravenous drug users.