

Chronic Liver Disease in the Hispanic Population of the United States

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This article has an accompanying continuing medical education activity on page e109. Learning Objectives—At the end of this activity, the learner will recognize the spectrum of liver disease in the Hispanic population in the United States, appreciate the importance of fatty liver disease and its progression to cirrhosis, and understand the role of viral hepatitis in the genesis of liver disease in the Hispanic US population.

Chronic liver disease is a major cause of morbidity and mortality among Hispanic people living in the United States. Environmental, genetic, and behavioral factors, as well as socioeconomic and health care disparities among this ethnic group have emerged as important public health concerns. We review the epidemiology, natural history, and response to therapy of chronic liver disease in Hispanic patients. The review covers nonalcoholic fatty liver disease, viral hepatitis B and C, coinfection of viral hepatitis with human immunodeficiency virus, alcoholic cirrhosis, hepatocellular carcinoma, autoimmune hepatitis, and primary biliary cirrhosis. For most of these disorders, the Hispanic population has a higher incidence and more aggressive pattern of disease and overall worse treatment outcomes than in the non-Hispanic white population. Clinicians should be aware of these differences in caring for Hispanic patients with chronic liver disease.

Keywords: Ethnicity; Fibrosis; Race; Latino; Risk; Epidemiology.

The Hispanic population is the largest and fastest growing minority group in the United States. Currently they comprise 15% of the United States population and by the year 2050 will be 30% of the population.¹ The Census Bureau classifies Hispanic as an ethnic group and considers the terms Hispanic, Latino, and Spanish as synonymous. Hispanic persons can be of any racial background and represent a heterogeneous population with multiple origins, cultures, and genetic backgrounds including people of Mexican, Puerto Rican, Cuban, Central or South American, or other Spanish culture or origin. Mexican Americans comprise 65% of the United States Hispanic population, followed by Central and South Americans (17.4%), Puerto Ricans (8.6%, not including the 4.2 million people living on the island of Puerto Rico), and Cuban Americans (4%).¹ Most Hispanic persons now living in the United States were born in the United States and less than one-third of Hispanic persons residing in the United States are immigrants.² On average, Hispanic persons living in the United States have a socioeconomic status equivalent to African American people, but mortality rates that are comparable to those of non-Hispanic White (NHW) persons and considerably better than the African American population.^{3–5} Furthermore, life expectancy among Hispanic people is on average 3 years greater than in NHW people. These epidemiologic characteristics of low socioeconomic sta-

tus but favorable overall health outcomes are commonly referred to as “the Hispanic paradox.”

Despite the overall survival advantage for Hispanic persons, they are at increased risk for certain diseases including chronic liver disease. Data from the United States National Center for Health Statistics (2000–2006) identified chronic liver disease as the sixth most common cause of death in the Hispanic population.⁶ In contrast, liver disease is not included among the 10 most frequent causes of mortality in NHW and African American populations. Mortality from chronic liver disease in Hispanic people in the United States is nearly 50% higher than in NHW persons (13.7 per 100,000 in Hispanic persons vs 9.2 in NHW and 7.5 in African American persons).⁷ Furthermore, while mortality rates from chronic liver disease in the United States progressively declined during the past decade, this trend was not evident in the Hispanic population.⁸ These ethnic differences in liver disease burden remain poorly understood but variations in behavioral patterns, healthcare access, referral to specialists, and utilization of therapeutic interventions have all been proposed as potential explanations for these less favorable outcomes in Hispanic persons.^{9–11}

Methods

We searched the MedLine database to identify relevant studies. The Medical Subject Heading terms “Hispanic American” (which encompasses Hispanic, Latino, Mexican American, Spanish American, Cuban American, Puerto Rican, and persons from Central or South America, or other Spanish culture or origin), “Ethnic Groups,” and “Population Groups” were combined with the Boolean operator “AND” to the search terms “chronic liver disease,” “cirrhosis,” “nonalcoholic fatty liver disease,” “NAFLD,” “nonalcoholic steatohepatitis,” “NASH,” “viral hepatitis,” “hepatitis B,” “hepatitis C,” “HIV,” “alcoholic liver disease,” “alcoholic cirrhosis,” “hepatocellular carcinoma,” “hepatoma,” “autoimmune hepatitis,” “primary biliary cirrho-

Abbreviations used in this paper: AIH, autoimmune hepatitis; HBV, hepatitis B virus; HCC, hepatocellular carcinoma; HCV, hepatitis C virus; HIV, human immunodeficiency virus; NAFLD, nonalcoholic fatty liver disease; NHANES, National Health and Nutrition Examination Survey; NHW, non-Hispanic white; PBC, primary biliary cirrhosis; PSC, primary sclerosing cholangitis; SEER, surveillance epidemiology and end results; SVR, sustained virologic response.

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1542-3565/\$36.00

doi:10.1016/j.cgh.2011.04.027

sis,” and “primary sclerosing cholangitis.” The Related Articles function of PubMed was used to cross-check for additional relevant studies. The searches were also supplemented by screening the reference lists of included studies and reviews to identify any additional publications missed by the database searches. We limited the literature search to English- and Spanish-language publications. A total of 90 publications were included in the review.

Results

Hispanic people living in the United States exhibit singular variations in epidemiology, natural history, and response to therapy of chronic liver disease. Nonalcoholic fatty liver disease (NAFLD) is the most prevalent chronic liver disease in Hispanic persons followed by chronic alcoholic liver disease and viral hepatitis C and B.¹²⁻¹⁵ Among Hispanic persons, hepatocellular carcinoma also has a higher incidence and worse prognosis than NHW or African American persons.^{16,17} Data on ethnic-specific characteristics of less prevalent diseases such as autoimmune hepatitis and cholestatic liver diseases are limited; however, preliminary genetic characteristics and differences in the severity of these diseases have been found among Hispanic persons.

Nonalcoholic Fatty Liver Disease

The most extensive literature on chronic liver disease among Hispanic persons is available for NAFLD. This disease is now recognized as the most frequent etiology of elevated serum aminotransferase levels in the United States and is associated with ethnic-specific differences in body habitus, biochemical, and physiological characteristics.^{18,19} Multiple studies have shown that NAFLD is more common in Hispanic than in NHW or African American persons of the same age with an even distribution among Hispanic men and women.^{12,18,20-22} Studies measuring hepatic triglyceride content by magnetic resonance spectroscopy identified steatosis in 45% of the Hispanic population, making NAFLD 1.4 times more frequent in Hispanic than in NHW and 1.9 times more common than in African American persons.¹² Multiple other studies also support this ethnic-related distribution of the prevalence of the disease.^{18,21,22} One limitation of current epidemiologic data is that the prevalence of NAFLD has typically been estimated using imaging studies, either to establish a presumptive diagnosis or to screen individuals subsequently evaluated with liver biopsy. For example, Williams et al²³ reported the ethnic distribution of biopsy-proven NAFLD in a cohort of patients with abnormal liver ultrasounds. Similar to previous reports, Hispanic persons had the highest prevalence of NAFLD (58.3%), followed by Caucasian (44.4%), and African American (35.1%) persons.²³

The most commonly accepted explanation for these epidemiologic variations reflects ethnic differences in prevalence of the metabolic syndrome.²⁴ Data from the National Health and Nutrition Examination Survey (NHANES) indicate that the prevalence of the metabolic syndrome is strikingly higher in Hispanic than in NHW and African American persons (31.9%, 23.8%, and 21.6%, respectively).²⁵ Furthermore, obesity and insulin resistance, 2 important risk factors for the metabolic syndrome, have been found to have a positive correlation with hepatic steatosis in Hispanic persons only.¹⁸ Insulin resistance is strongly associated with intraperitoneal fat content, and

Hispanic persons living in the United States also have the highest intraperitoneal and hepatic fat content when compared with African American and NHW persons.^{25,26}

Histologic and serologic characteristics of NAFLD in different ethnic groups have been noted. For example, a retrospective analysis of liver biopsies revealed that Hispanic persons more frequently had Mallory bodies, more pronounced hepatocyte ballooning, and more advanced fibrosis than NHW or African American persons.²² Hispanic persons with NAFLD also have higher levels of aminotransferases, therefore suggesting a more prominent inflammatory process during the disease. Furthermore, age and an aspartate aminotransferase/alanine aminotransferase ratio ≥ 1 are independent predictors of advanced fibrosis or cirrhosis only among Hispanic persons.²⁷ However, the severity of liver disease (measured by fibrosis score) is similar in Hispanic and NHW persons with NAFLD. Interestingly, African American persons with NAFLD have lower rates of steatosis, less severe fibrosis, and slower progression to non-alcoholic steatohepatitis (NASH) and cirrhosis than Hispanic persons.²⁸

Although multiple environmental risk factors may be responsible for ethnic variations in NAFLD, genetic differences are also implicated. For example, a recent study identified a novel polymorphism in a specific allele (rs738409 G) that encodes for the enzyme patatin-like phospholipase domain-containing protein 3 (*PNPLA3*), also known as adiponutrin, which is strongly associated with hepatic lipid content. Although the mechanisms by which this allele affects hepatic fat content remain to be elucidated, it is a predictor of the histologic severity of NAFLD with homozygote patients having a 2-fold greater hepatic fat content than noncarriers of the allele. Among ethnic groups, Hispanic persons have the highest frequency of this polymorphism (49%), followed by NHW (23%), and African American persons (17%).²⁹ A subsequent report demonstrated that this polymorphism was present in 91% of Hispanic persons and 70% of non-Hispanic persons with biopsy-proven NAFLD.³⁰

There is no Food and Drug Administration (FDA)-approved therapy for NAFLD; however, insulin sensitizers and antioxidants such as pioglitazone and vitamin E have been studied.^{31,32} To date, ethnic differences in response to therapy have not been reported. Current management of NAFLD focuses on weight loss, increased physical activity, and modification of metabolic risk factors. Existing data suggest that cultural, emotional, social, and linguistic issues are critical factors that need to be addressed in order for exercise programs and nutritional counseling interventions to be effective in Hispanic persons.³³ Outreach by community health workers is one promising approach to tackle these barriers by increasing participation and adherence.³⁴

The only definitive treatment for NAFLD is liver transplantation; however, to date there are no data comparing ethnic-specific differences in graft or patient survival, recurrence, or de novo development of the disease following liver transplantation.^{35,36}

Alcoholic Liver Disease

Data from the Centers for Disease Control and Prevention (CDC) implicate alcohol in 24% of newly identified cases of chronic liver disease in the United States.³⁷ Behavioral patterns of alcohol consumption vary extensively among Hispanic and

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