Original Article JOURNAL OF CLINICAL AND EXPERIMENTAL HEPATOLOGY

High Prevalence of Cirrhosis at Initial Presentation Among Safety-Net Adults with Chronic Hepatitis B Virus Infection

Elaine Tang [*], Sharon Torres [†], Benny Liu [†], Rachel Baden [‡], Taft Bhuket [†], Robert J. Wong [†]

[*]School of Medicine, Tufts University, Boston, MA, United States, [†]Division of Gastroenterology and Hepatology, Alameda Health System – Highland Hospital, Oakland, CA, United States and [‡]Department of Medicine, Alameda Health System – Highland Hospital, Oakland, CA, United States

Background and aims: **Delays in diagnosis of chronic hepatitis B virus infection (HBV) may be more common among underserved safety-net populations, contributing to more advanced disease at presentation. We aim to evaluate rates of and predictors of cirrhosis and cirrhosis-related complications among adults with chronic HBV.** ***Methods:*** **We retrospectively evaluated consecutive chronic HBV adults from gastroenterology clinics from July 2014 to May 2016 at a community-based safety-net hospital. Prevalence of cirrhosis or cirrhosis-related complications (ascites, variceal bleeding, hepatic encephalopathy (HE), hepatocellular carcinoma (HCC)) at initial presentation was stratified by sex and race/ethnicity. Predictors of cirrhosis or cirrhosis-related complications at presentation were evaluated with multivariate logistic regression.** ***Results:*** **Among 329 chronic HBV patients (mean age 49.1 years, 55.3% male, 66.5% Asian, 18.6% HBeAg positive) 27.7% had cirrhosis at presentation, 4.3% ascites, 3.7% variceal bleeding, 4.9% HE, and 4.0% HCC. Compared to women, men were more likely to have cirrhosis (34.6% vs. 19.1%, $P < 0.01$) and variceal bleeding (5.6% vs. 1.4%, $P < 0.05$) at presentation. On multivariate regression, older age at presentation (OR, 1.04; 95% CI, 1.01–1.07; $P = 0.003$) and positive HBeAg (OR, 2.57; 95% CI, 1.20–5.51; $P = 0.015$) were associated with higher odds of cirrhosis at presentation, whereas men had a non-significant trend toward higher odds of cirrhosis (OR, 1.88; 95% CI, 0.99–3.58; $P = 0.055$).** ***Conclusion:*** **Among adults with chronic HBV at an ethnically diverse safety-net hospital system, nearly 30% of patients had cirrhosis at initial presentation, with the greatest risk seen among patients of male sex, older age, and with positive HBeAg.** **(J Clin Exp Hepatol 2017;xx:1–6)**

Hepatitis B virus (HBV) infection is the leading cause of liver-disease related morbidity and mortality worldwide with over 250 million people living with the disease chronically.[1] Currently, HBV can be prevented with vaccines and managed effectively with antiviral therapy, and early diagnosis of HBV through effective screening programs allows for timely initiation of therapy to prevent disease progression.[2,3] However, Asia, sub-Saharan Africa, and the Middle East has the greatest chronic HBV prevalence, where it is often transmitted vertically and therapies are not as readily available.[4]

In the United States, areas with higher rates of HBV are often associated with a larger immigrant population as well, contributing to the 1.25 million cases of HBV in the United States, though this may even be an underestimation.[5,6] Despite clear guidelines from the American Association for the Study of Liver Disease (AASLD) for HBV screening and management, persistent lack of knowledge and awareness of HBV screening among primary care providers contributes to sub-optimal HBV care among the high risk populations.[7–9] This sub-optimal care may contribute to delays in linkage to appropriate treatment, allowing disease progression to cirrhosis and hepatocellular carcinoma (HCC). Cirrhosis is a particularly worrisome consequence of HBV because it has additional complications associated including ascites, variceal bleeding, hepatic encephalopathy (HE), and HCC. Nearly 40% of chronic HBV patients will develop cirrhosis or cirrhosis-related complications in their lifetime; however this risk can be mitigated with effective therapy aimed at viral suppression.[3] The financial burden of cirrhosis was estimated to be $13 billion in the United States, emphasizing the importance of early preventative care to reduce the incidence of cirrhosis and its strain on the healthcare system.[10,11] Unfortunately, delays in HBV and cirrhosis diagnosis, which may be more common among underserved

Keywords: viral hepatitis, disparities, linkage to care
Received: 10 October 2017; *Accepted:* 21 November 2017; *Available online:* xxx

Address for correspondence: Robert J. Wong, Assistant Clinical Professor of Medicine, Director of Research and Education, Division of Gastroenterology and Hepatology, Alameda Health System – Highland Hospital Campus, 1411 East 31st Street, Highland Hospital – Highland Care Pavilion 5th Floor, Endoscopy Unit, Oakland, CA 94602, United States. Tel.: +1 510 437 6531.
E-mail: Rowong@alamedahealthsystem.org

Abbreviations: AASLD: American Association for the Study of Liver Disease; HBV: hepatitis B virus; HCC: hepatocellular carcinoma; HE: hepatic encephalopathy

https://doi.org/10.1016/j.jceh.2017.11.009

Please cite this article in press as: Tang E, et al. High Prevalence of Cirrhosis at Initial Presentation Among Safety-Net Adults with Chronic Hepatitis B Virus Infection. *J Clin Exp Hepatol.* (2017), https://doi.org/10.1016/j.jceh.2017.11.009

safety-net populations, contribute to more severe disease at presentation, which contributes to greater morbidity and mortality.[7–9,12–14]

Safety-net systems provide care to the indigent communities of the geographic region. The majority of patients served among safety-net systems either have no insurance or are underinsured. Among those that do have insurance, the majority are covered by Medicaid or other state-sponsored insurance plans. There is a high prevalence of ethnic minorities among safety-net systems and majority live at or below the national poverty level. Our current study aimed to evaluate rates of and predictors of cirrhosis and cirrhosis-related complications among adults with chronic HBV at first encounter with specialty care in an ethnically diverse, safety-net population.

METHODS

We retrospectively evaluated consecutive chronic HBV adults seen at gastroenterology clinics from July 2014 to May 2016 at a large community-based safety-net hospital system to determine the prevalence and predictors of cirrhosis and cirrhosis related complications (ascites, variceal bleeding, HE, or HCC) at initial presentation. The diagnosis of cirrhosis was determined through a thorough review of the electronic medical records and incorporated data from the clinical history from inpatient and outpatient chart notes, laboratory data, radiographic data, and liver biopsy data if available. Our diagnosis was not based on diagnosis coding or billing coding, but rather based on thorough chart review by a clinician to interpret and identify the diagnosis of cirrhosis. Thus the inclusion of cirrhosis on the problem list or discharge diagnoses by the treating provider was used to confirm presence of cirrhosis. Nonalcoholic fatty liver disease (NAFLD) was determined in a similar fashion, such that we relied on the clinical notes, and if NAFLD was listed as a diagnosis, we considered the HBV patients to have concurrent NAFLD. In a similar fashion the presence of ascites, variceal bleeding, HE, and HCC was determined. For HCC in particular, the diagnosis relied on radiographic confirmation based on established AASLD criteria.

Overall patient demographics were stratified by sex and presented as proportions and frequencies or mean and standard deviation as appropriate. The prevalence of cirrhosis and cirrhosis-related complications at presentation were stratified by sex, race/ethnicity (Asian vs. non-Asian), HBeAg status (HBeAg positive vs. HBeAg negative) and evaluated with chi-square testing. Predictors of presenting with cirrhosis or cirrhosis-related complications at initial encounter were evaluated with multivariate logistic regression models. Variables chosen for inclusion in the multivariate model were selected a priori based on what we hypothesized to be clinically significant. The final multivariate model included age, sex, race/ethnicity, HBeAg status, and presence of concurrent nonalcoholic fatty liver disease. Statistical analyses were performed using Stata statistical software package (version 13.0) and statistical significance was met with P-value < 0.05. This study was approved by Alameda Health System Institutional Review Board.

RESULTS

Among 329 patients with chronic HBV included in the study, 55.3% ($n = 182$) were male and 66.5% ($n = 218$) identified as Asian race/ethnicity (Table 1). The average age of all the patients was 49.1 ± 13.1 years, and the average body mass index was 25.2 ± 6.2. 18.6% ($n = 44$) were HBeAg positive and 35.9% of patients had concurrent nonalcoholic fatty liver disease. 28.7% of chronic HBV had concurrent hypertension, 17.7% had concurrent diabetes mellitus, and 18.5% had concurrent metabolic syndrome. With the exception of age at time of presentation (males 50.8 years vs. females 46.9 years, $P < 0.01$), no significant sex-specific differences in patient characteristics were observed (Table 1).

Overall, 27.7% of chronic HBV patients had evidence of cirrhosis at time of initial presentation (Figure 1). When stratified by sex, males were significantly more likely to have cirrhosis at presentation compared to females (34.6% vs 19.1%, $P < 0.01$) and males were also more likely to have variceal bleeding at presentation (5.6% vs 1.4%, $P < 0.05$) (Figure 1, Table 2). HBeAg positive patients were significantly more likely to have cirrhosis at presentation compared to HBeAg negative patients (38.6% vs 23.9%, $P < 0.05$). No significant difference in prevalence of cirrhosis was observed when comparing non-Asians vs Asians (Figure 1). No other significant differences in prevalence of cirrhosis-related complications such as ascites, variceal bleeding, hepatic encephalopathy, or hepatocellular carcinoma were observed (Table 2).

On multivariate regression analysis, older age (OR, 1.04; 95% CI, 1.01–1.07; $P = 0.003$) and HBeAg positivity (OR, 2.57; 95% CI, 1.20–5.51; $P = 0.015$) were associated with significantly higher odds of cirrhosis at initial presentation (Table 3). There was a non-significant trend toward higher odds of cirrhosis at presentation among males compared to females with chronic HBV (OR, 1.88; 95% CI 0.99–3.58; $P = 0.055$) (Table 3). When evaluating odds of cirrhosis-related complications at time of presentation, presence of cirrhosis was associated with significantly higher odds of ascites (OR, 21.87; 95% CI, 2.23–214.70; $P = 0.008$), variceal bleeding (OR, 33.59; 95% CI, 3.90–289.37; $P = 0.001$), HE (OR, 28.10; 95% CI, 3.39–232.91; $P = 0.002$), and HCC (OR, 24.62; 95% CI, 2.81–215.92; $P = 0.004$) at time of presentation. However, no other significant predictors of cirrhosis-related complications were observed.

Please cite this article in press as: Tang E, et al. High Prevalence of Cirrhosis at Initial Presentation Among Safety-Net Adults with Chronic Hepatitis B Virus Infection. *J Clin Exp Hepatol.* (2017), https://doi.org/10.1016/j.jceh.2017.11.009