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Brief report

BRIEF REPORT

Improved hepatitis A and hepatitis B vaccination strategy is necessary for patients with chronic hepatitis C

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Introduction

Hepatitis C virus (HCV) is a major cause of chronic liver diseases. Hepatitis A virus (HAV) or hepatitis B virus (HBV) infection on pre-existing hepatitis C can lead to significant morbidity and mortality [1]. The Advisory Committee on Immunization Practices (ACIP) recommends HAV and HBV vaccination for patients with chronic liver diseases [2, 3]. Best-practice advice from the American College of Physicians and the Centers for Disease Control and Prevention (CDC) also emphasized the importance of HBV vaccination for at-risk populations [4]. The hepatitis B vaccine response, however, is generally lower among patients with chronic liver diseases, especially those with cirrhosis or older age [5, 6]. In this study, we reported that a high proportion of patients with chronic hepatitis C remained at risk of HAV or HBV infection at their referral to our tertiary Liver Center.

Methods

A systematic review of online medical records was performed to identify unique patients with chronic hepatitis C evaluated at Beth Israel Deaconess Medical Center (BIDMC) between 1998 and 2019. Patients with HIV coinfection were excluded. Clinical, demographic information, HAV, and HBV serological results from their initial clinic visits at BIDMC were recorded. For this analysis, 'HAV-immune' indicated patients with positive anti-HAV from previous vaccination or natural exposure and 'HAV-susceptible' included those anti-HAV-negative patients. 'HBV-susceptible' referred to those who tested negative for HBsAg, anti-HBs, and anti-HBc. The prevalence of HAV, HBV susceptibility was compared between the periods 1998–2008 and 2009–2019. The study was approved by the Institutional Review Board at BIDMC.

Results

A total of 4,010 patients with chronic hepatitis C were identified and 2,740 (68.3%) had complete HBV serological test results. Among them, 1,027 (37.5%) had either chronic hepatitis B or previous HBV exposure at the time of referral, 664 (24.2%) had evidence of vaccine response with anti-HBs (+), and the remaining 1,049 (38.3%) were susceptible to HBV infection. HAV serological results were available in 1,627 (40.6%) patients. Only 839 (51.6%) had HAV immunity and 788 (48.4%) were still at risk of HAV infection.

The following HBV-status analysis excluded those patients with chronic hepatitis B or previous HBV exposure and focused on the remaining 1,713 subjects. This cohort had predominantly male patients (n = 1,081, 63.1%) with an average age of 47.5 (ranged 18–90) years. Based on self-identification, there were 1,261 Caucasians (73.6%), 209 African Americans (12.2%), 68 Hispanic subjects (4.0%), 67 Asians (3.9%), and 108 undefined (6.3%). The presence (n = 570) or absence (n = 1,089) of cirrhosis was documented in 1,659 out of 1,713 (96.8%) patients. HBV status is presented in Table 1. At referral, 1,049 of the 1,713 (61.2%) HCV patients without history of prior HBV exposure were susceptible to HBV infection; the proportions of susceptible male (62.4%) and female (59.2%) were similar. Overall, non-Whites had higher rates of anti-HBs positivity indicative of prior vaccine response compared to Whites. Only 21.4% (142/664) of the

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Table 1. Hepatitis B virus (HBV)-susceptible status in patients with chronic hepatitis C[a]

Characteristic	No. of patients	HBV-susceptible, *n* (%)	*P*-value
Sex			0.18
Male	1,081	675 (62.4)	
Female	632	374 (59.2)	
Race			<0.001
Asian	67	28 (41.8)	
Hispanic	68	39 (57.4)	
African American	209	103 (49.3)	
White	1,261	808 (64.1)	
Period			0.06
1998–2008	512	331 (64.6)	
2009–2019	1,201	718 (59.8)	
Patients with cirrhosis			0.94
1998–2008	154	116 (75.3)	
2009–2019	416	312 (75.0)	
Patients >40 years of age			0.68
1998–2008	417	278 (66.7)	
2009–2019	845	573 (67.8)	

[a]Patients with chronic hepatitis B or prior HBV exposure were excluded.

Table 2. Hepatitis A virus (HAV)-susceptible status in patients with chronic hepatitis C

Characteristic	No. of patients	HBV-susceptible, *n* (%)	*P*-value
Sex			0.31
Male	1,024	486 (47.5%)	
Female	603	302 (50.1%)	
Race			<0.001
Asian	63	18 (28.6%)	
Hispanic	66	21 (31.8%)	
African American	202	81 (40.1%)	
White	1,197	619 (51.7%)	
Period			0.001
1998–2008	500	210 (42.0%)	
2009–2019	1,127	578 (51.2%)	
Patients with cirrhosis			0.032
1998–2008	152	56 (36.8)	
2009–2019	400	188 (47.0)	
Patients >40 years of age			0.038
1998–2008	408	170 (41.7)	
2009–2019	786	377 (48.0)	

patients with evidence of vaccine response were cirrhotic. Since vaccination records were not available, we could not determine the rate of prior nonresponse or incomplete vaccination. The proportion of patients susceptible to HBV was highest among Whites (64.1%), followed by Hispanics (57.4%), African Americans (49.3%), and Asians (41.8%). The rates of HBV susceptibility were similarly high for the two study periods (64.6% vs 59.8%, $P = 0.06$). More than 75% cirrhotic patients and ≥65% patients over 40 years of age were susceptible to HBV in both study decades.

HAV status is presented in Table 2. Seven hundred and eighty-eight of the 1,627 (48.4%) HCV patients were susceptible to HAV infection during their first visits to the Liver Center; the rates were similar for males (47.5%) and females (50.1%). The proportion of patients susceptible to HAV was highest among Whites (51.7%), followed by African Americans (40.1%), Hispanics (31.8%), and Asians (28.6%). The prevalence of those who remained at risk of HAV infection was higher in the later period (2009–2019) than in the earlier decade (1998–2008) (51.2% vs 42.0%, $P = 0.001$). There were also greater proportions of HAV-susceptible patients with cirrhosis ($P = 0.001$) or ≥40 years of age in the later period ($P = 0.038$).

Discussion

With the availability of direct-acting antiviral therapy for chronic hepatitis C, the eradication of HCV is a reality. Superinfection with HAV and HBV remains a significant concern. Despite recommendations from ACIP and CDC, the HBV-immunization rate for chronic hepatitis C patients is suboptimal [6]. Harris *et al.* [7] reported that only 55% of HCV patients had complete HBV serological testing at an urban health system and 27% remained susceptible to HBV infection. Our results showed a similar trend with a 68% HBV-testing rate and 38% HBV-susceptible at referral. The rates of anti-HBs positivity were similarly low in the past two decades. This might imply that the HBV-vaccination practice has not improved in the primary-care setting over time. Only about 20% of the patients with HBV-vaccine response had cirrhosis. Reduced vaccine response among patients with advanced liver disease could also be a contributing factor [7]. A large proportion of the HCV patients susceptible for HBV infection in this study had cirrhosis and were >40 years of age; these patients would also have poor liver-disease prognosis if they acquired HBV coinfection [8]. Interestingly, non-Whites were found to have significantly higher rates of anti-HBs positivity from vaccination. The acceptance and awareness of HBV vaccination among patients and health providers in the various ethnic groups might account for the discrepant vaccine-response rates.

HAV immunity cannot be distinguished from HAV-vaccine response and natural infection. Approximately 50% of the HCV patients remained susceptible to HAV superinfection. The prevalence of HAV immunity was higher among non-Whites and in the earlier study period. This could be due to a higher rate of natural HAV infection among immigrant populations.

In conclusion, our observations support the need for increased HAV and HBV testing and vaccination awareness, especially among the primary-care physicians. Acceptance of vaccination among patients with diverse cultural backgrounds is also important to explore. Since patients with chronic liver disease, especially those with advanced fibrosis, tend to have a suboptimal HBV-vaccine response, complete vaccine series with post-vaccination testing are highly recommended [9].

Authors' contributions

M.H.M.: study design, data collection/ analysis, writing and revising the manuscript; H.K.: manuscript writing and data collection/analysis; S.P.K: manuscript writing and data collection; K.J.C.R: data collection; J.G: data collection; P.A.S.: data collection; A.T.: manuscript writing; D.T.Y.L: study concept, data analysis, manuscript writing and revision.

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Conflicts of interest

None declared.

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