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BRIEF REPORT

Chronic Hepatitis B Infection Among Preexposure Prophylaxis Users Enrolled in a Population-Based Program in British Columbia, Canada

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Initiation of human immunodeficiency virus preexposure prophylaxis (PrEP) medications will also treat hepatitis B infection (HBV). The prevalence of chronic HBV was 0.86% (n = 41/4760) among enrollees in a provincial PrEP program in British Columbia, Canada. Overall, 46.3% lacked follow-up HBV DNA monitoring, underscoring the need for HBV-related education for PrEP prescribers.

Keywords. emtricitabine/tenofovir disoproxil fumarate; hepatitis B; HIV PrEP; HIV prevention; MSM.

Emtricitabine (FTC)/tenofovir disoproxil fumarate (TDF)–based preexposure prophylaxis (PrEP) is now recommended as standard of care for prevention in individuals at high risk for human immunodeficiency virus (HIV) infection [1–3]. Determination of hepatitis B virus (HBV) status for individuals initiating PrEP is essential as both FTC and TDF have HBV antiviral activity. As such, current clinical PrEP guidelines recommend baseline evaluation of HBV status [2, 3]. In individuals living with chronic HBV, both evaluation of baseline fibrosis stage to determine need for therapy and on-treatment monitoring for response are recommended [4]. Abrupt cessation of therapy may lead to risk for hepatitis flare, further necessitating expert management [5, 6]. There is limited clinical experience with the use of PrEP in those living with chronic HBV as this was an exclusion criterion for most of the original PrEP clinical trials [7, 8]. The iPrEx study included individuals living with HBV, but only 6/2499 (0.25%) received FTC/TDF [1, 9]. Given the relative paucity of clinical data, we sought to characterize baseline HBV status and monitoring among individuals receiving PrEP through a province-wide program in British Columbia (BC), Canada.

METHODS

The BC PrEP Program

The BC Centre for Excellence (BC-CfE) in HIV/AIDS offers a publicly-funded HIV PrEP program to all residents of BC deemed clinically at high risk for HIV infection according to provincial PrEP guidelines [10]. This program was launched in January 2018 to complement the existing HIV Treatment as Prevention Strategy (TasP) and provides FTC/TDF to eligible residents. Tenofovir alafenamide is not routinely covered in the provincial PrEP program. Eligibility criteria include an HIV Incidence Risk Index for Men Who Have Sex With Men (HIRI-MSM) score ≥10, condomless anal sex and prior history of infectious syphilis or rectal bacterial sexually transmitted infection (STI), recurrent use of HIV postexposure prophylaxis, or an ongoing sexual/injection drug use relationship with an HIV-positive partner who is not receiving stable and effective antiretroviral therapy (ART).

Study Population

The study population was made up of individuals enrolled in the BC-CfE HIV PrEP program from January 2018 to June 2019 and followed until 31 August 2019. To access PrEP, health care providers were required to document HBV status (HBV surface antigen [HBsAg] status as positive or negative) during the enrollment process. The BC-CfE PrEP program has ongoing linkage with data obtained from the St Paul's Hospital/Providence Health Care laboratory interface in Vancouver, BC. Of note, the St Paul's Virology Laboratory performs all HBV DNA monitoring for the province.

We evaluated the prevalence of HBV defined based on physician report as indicated on a PrEP Enrollment and Prescription Request Form or documented baseline HBsAg in the St Paul's Virology Laboratory system. Individuals with an isolated HBV core antibody were therefore not included. Baseline was defined as any available result 6 months prior to 3 months following PrEP initiation. We compared baseline demographic characteristics including median age, gender, PrEP-qualifying risk factors, and urban vs rural location (based on 3-digit postal code) between those with and those without HBV, using χ^2, Fisher exact, or Kruskal-Wallis tests. We assessed the proportion of HBV-positive individuals who underwent evaluation of

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HBV DNA status at baseline and at any time over the follow-up period, as a measure for engagement in HBV care.

Patient Consent Statement

Analyses from the BC-CfE Drug Treatment Program are approved under the University of British Columbia–Providence Healthcare Research Ethics Board (H05-50123).

RESULTS

The study population included 4760 individuals with a median age of 33 years (25th–75th percentile [Q1–Q3], 27–43 years) and consisted of 4680 (98.3%) males, 24 (0.5%) females, 53 (1.1%) transgender people, and 3 (0.06%) of unknown gender. There were 4686 (98.4%) individuals identifying as MSM, and 285 (5.9%) were reported as having a known HIV-positive partner not on stable or effective ART. Of 4310 (90%) PrEP recipients with a reported HIRI-MSM score, the median score was 19 (Q1–Q3, 15–24), and 955 (20.0%) were reported as having a prior bacterial rectal STI or syphilis infection. Most individuals (4559 [95.7%]) were from an urban area. Only 298 (6.2%) individuals were formally prescribed PrEP for use on an intermittent/on-demand basis, while 4462 (93.7%) were prescribed PrEP for daily use.

Hepatitis B Status

There were 19 laboratory-confirmed HBV cases among 1845 individuals in the overall cohort where laboratory results were available. Among the remaining 2915 individuals with missing laboratory data, an additional 22 physician-reported HBV infections were identified, for an overall HBV prevalence of 0.86% (n = 41/4760). There were an additional 4 individuals reported to have HBV who were documented to be HBsAg-negative; these individuals were not considered to have HBV for this analysis.

The median baseline alanine aminotransferase (ALT) level for those with HBV was 44 IU/mL (Q1–Q3, 27–66 IU/mL); 17.0% had ALT greater than the upper limit of normal, compared with 4.5% for those without HBV ($P = .005$). Of the 19 individuals with confirmed HBsAg-positive status, only 8 (42.1%) were tested for HBV e antigen (n = 2/8 [25%] positive), and 13 (68.4%) were tested for HBV e antibody (n = 11/13 [84.6%] positive).

Of the 41 individuals who were recorded as being HBV-positive, 29 (70.7%) had at least 1 HBV DNA measurement, with 27 (65.8%) having a baseline HBV DNA measurement. Repeat HBV DNA measurements occurred in 22 (53.7%) individuals, with 95% (n = 21/22) achieving viral suppression (<25 IU/mL) over the study period.

When comparing PrEP participants with chronic HBV infection and those without, in our bivariate analysis we found very few differences. The only statistically significant difference was in the prevalence of reported prior bacterial rectal STI or syphilis, which was lower in HBV-positive individuals (7.3% vs 20.1%; $P = .048$). There were no statistically significant differences in median age, gender, urban vs rural location, HIRI-MSM score, or other PrEP-qualifying criteria (Table 1).

Throughout the study period, 1 (2.4%) individual among the 41 with HBV was formally prescribed intermittent PrEP, which is considered inadequate in the context of chronic HBV infection. One (2.4%) individual experienced a gap in PrEP prescription supply >6 months compared with 132 (2.8%) among the 4719 without HBV ($P = .999$).

DISCUSSION

To our knowledge, this is the largest clinical experience of PrEP use in individuals with chronic HBV. In our study of >4000 individuals accessing PrEP in BC, the prevalence of chronic HBV infection was just below 1%. The prevalence of chronic HBV in

Table 1. Bivariate Analysis of Factors Associated With Chronic Hepatitis B Infection at Time of Enrollment in the British Columbia Human Immunodeficiency Virus Preexposure Prophylaxis Program

	Reported/Laboratory-Confirmed Hepatitis B Status			Laboratory-Confirmed Hepatitis B Status		
Characteristic	HBV Positive (n = 41)	HBV-Negative (n = 4719)	*P* Value	HBV-Positive (n = 19)	HBV-Negative (n = 1826)	*P* Value
Age, y, median (Q1–Q3)	39 (29–47)	33 (27–43)	.112	37 (29–44)	31 (26–39)	.138
Gender, male	40 (97.5)	4654 (98.6)	.422	18 (94.7)	1810 (99.1)	.144
MSM	41 (100)	4645 (98.4)	.999	19 (100)	1800 (98.5)	.999
Urban address at time of enrollment	40 (97.5)	4519 (95.7)	.999	18 (94.7)	1745 (95.5)	.999
HIRI-MSM Risk Index, median (Q1–Q3)	18 (14–20)	19 (15–24)	.080	16.5 (13.5–23)	19 (15–25)	.165
HIRI-MSM Risk Index >25	3 (7.3)	758 (16.0)	.330	2 (10.5)	328 (17.9)	.751
History of prior STI	3 (7.3)	952 (20.1)	.048	1 (5.2)	361 (19.7)	.286
PrEP use due to HIV-positive partner	1 (2.4)	284 (6.0)	.514	0	105 (5.7)	.626
Intermittent/on-demand PrEP prescription	1 (2.4)	297 (6.2)	.516	1 (5.2)	130 (7.1)	.999

Data are presented as No. (%) unless otherwise indicated. Factors were compared using χ^2, Fisher exact, or Kruskal-Wallis test.

Abbreviations: HBV, hepatitis B virus; HIRI, HIV Incidence Risk Index; HIV, human immunodeficiency virus; MSM, men who have sex with men; PrEP, preexposure prophylaxis; Q1, first quartile; Q3, third quartile; STI, sexually transmitted infection.