Continuum of Hepatitis B Surface Antigen Expression among PWID and MSM Living with HIV in India

768

Talia A Loeb[1], Mihili P Gunaratne[1], Hussain Syed Iqbal[2], Mark Anderson[3], A.K. Srikrishnan[2], Allison M McFall[1], Gregory M Lucas[4], Mary Rodgers[3], Muniratnam S Kumar[2], David Thomas[4], Ashwin Balagopal[3], Shruti H Mehta[1], Sunil S Solomon[4], Gavin Cloherty[3], Chloe Thio[4]

[1]Johns Hopkins Bloomberg School of Public Health, Baltimore, Maryland, USA, [2]YRG Care, Chennai, India, [3]Abbott Laboratories, Abbott Park, Illinois, USA, [4]Johns Hopkins University School of Medicine, Baltimore, Maryland, USA

BACKGROUND

- People who inject drugs (PWID) and men who have sex with men (MSM) are at particularly high risk for hepatitis B virus (HBV) and HIV acquisition
- Functional HBV cure: clearance of HBV surface antigen (HBsAg) from blood
  - More common among people with HIV/HBV taking tenofovir-based antiretroviral therapy (ART) than people with HBV mono-infection on tenofovir, suggesting that HBsAg "clearance" is not binary
    - HBsAg clearance may occur across a continuum of immunological control that is reduced by HIV and restored by ART

OBJECTIVE

- To characterize HBV and HIV biomarkers in people co-infected with HBV and HIV with varying HBsAg levels using an ultrasensitive HBsAg assay.

METHODS

- 2198 PWID and MSM living with HIV enrolled as part of a cluster randomized trial (total enrollment 2314)
- HBV biomarkers measured from stored plasma in 2198 participants (ARCHITECT platform): core antibody (anti-HBc), surface antibody (anti-HBs) and HBV DNA.
- HBsAg measured with ARCHITECT HBsAg Next Qualitative assay (HBsAg Nxt),
  - Negative = signal-to-cutoff (S/Co) <1
  - Limit of detection = 0.005 IU/mL
  - S/Co = 10 ~0.05 IU/mL, the sensitivity of most available assays
- Ever infected with HBV = anti-HBc reactive or HBsAg Next S/Co > 1
- HBsAg Nxt S/Co between 1 and 10 were specifically analyzed
- Descriptive statistics identified prevalence of occult HBV and detectable HBV DNA
- Multivariable logistic regression identified correlates of detectable HBV DNA

RESULTS

Table 1. Participant characteristics of PWID and MSM living with HIV and tested for HBV (N=2314) (N=2198

Median (IQR)/ n (column %)	Total (n=2198)	PWID (n=1126)	MSM (n=1072)
Age	30 (25, 37)	29 (24, 35)	32 (26, 40)
Male Sex	205 (93.4)	987 (87.7)	1072 (100)
Currently Married	991 (45.1)	413 (36.7)	578 (53.9)
At least a high school education	449 (20.4)	153 (13.6)	296 (27.6)
Unemployed	571 (26.0)	406 (36.1)	165 (15.4)
Homelessness, Past 6 Months	128 (5.8)	116 (10.3)	12 (1.1)
Alcohol Dependence	478 (21.8)	281 (25.0)	197 (18.4)
Ever infected with HBV (n=2198)	1354 (61.6)	851 (75.6)	503 (46.9)
HBsAg Next S/Co between 1 and 10 and non-missing HBV DNA	73 (5.4)	44 (5.2)	29 (5.8)

- **Among those who were positive for anti-HBc and had HBsAg Nxt ≥ 1 (n=257)**
  - 87 (33.8%) had HBsAg Nxt between 1-10, of whom 14 (16.1%) were missing the HBV DNA measure. Of the remaining 73, 44 were PWID and 29 were MSM (Table 2). 37% (n=27/73) had detectable HBV DNA

Functional cure of HBV may not be binary but rather represents a continuum of the quantity of HBsAg in plasma

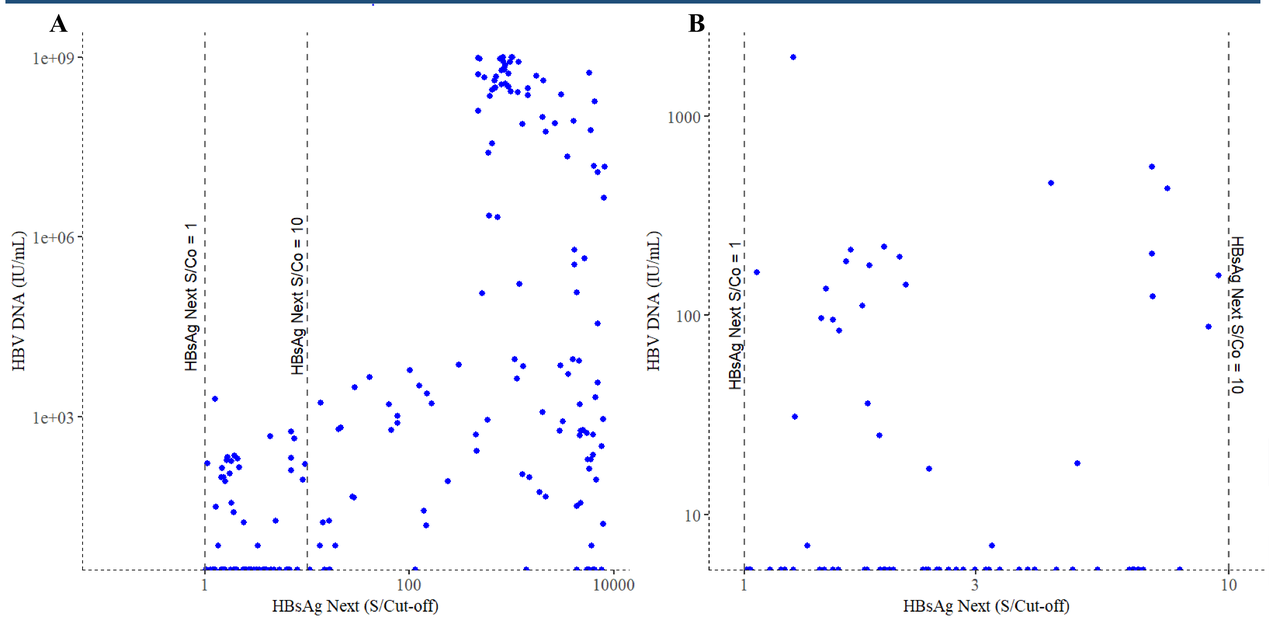


Figure 1. Spectrum of HBsAg Control among those reactive for anti-HBc or HBsAg Next S/Co >1. **A.** HBV DNA levels vs. HBsAg Next S/Co. **B.** Enlarged view of HBV DNA values for specimens with HBsAg Next S/Co values between 1 and 10 ("Occult HBV") – 37% of those with values of HBsAg Next S/Co between 1 and 10 had detectable HBV DNA and would have been classified as occult HBV.

Table 2. Participant Characteristics of PWID and MSM living with HIV and with HBsAg Nxt between 1 and 10 (n=73)

n (column %) / median (IQR)	Total (n=73)		PWID (n=44)		MSM (n=29)	
	Undetectable HBV DNA (n=46/73 = 63%)	Detectable HBV DNA (n=27/73=37%)	Undetectable HBV DNA (n=25/44=57%)	Detectable HBV DNA (n=19/44=43%)	Undetectable HBV DNA (n=21/29=72%)	Detectable HBV DNA (n=8/29=28%)
Age	30.5 (25, 39)	32 (26, 41)	30 (26, 37)	31 (24, 35)	31 (25, 40)	46 (31, 49)
Sex						
Male	38 (82.6)	26 (96.3)	17 (68.0)	18 (94.7)	21 (100)	8 (100)
Female	8 (17.4)	1 (2.7)	8 (32.0)	1 (5.3)	0 (0)	0 (0)
Marital Status						
Never Married	14 (30.4)	12 (44.4)	8 (32.0)	9 (47.4)	6 (28.6)	3 (37.5)
Married	28 (60.9)	13 (48.1)	16 (64.0)	8 (42.1)	12 (57.1)	5 (62.5)
Widowed/Divorced/Separated	4 (8.7)	2 (7.4)	1 (4.0)	2 (10.5)	3 (14.3)	0 (0)
Education						
No schooling	8 (17.4)	7 (25.9)	5 (20.0)	3 (15.8)	3 (14.3)	4 (50.0)
Primary/Secondary School	29 (63.0)	17 (45.9)	19 (76.0)	14 (73.7)	10 (47.6)	3 (37,5)
High school or above	9 (19.6)	3 (11.1)	1 (4.0)	2 (10.5)	8 (38.1)	1 (12.5)
Unemployed	15 (32.6)	7 (25.9)	13 (52.0)	4 (21.0)	2 (9.5)	3 (37.5)
Homelessness, Past 6 Months	2 (4.3)	2 (7.4)	2 (8.0)	2 (10.5)	0 (0)	0 (0)
Alcohol Dependence	10 (21.7)	4 (14.8)	9 (36.0)	2 (10.5)	1 (4.8)	2 (25.0)
Initiated on ART	21 (45.6)	4 (14.8)	10 (40.0)	4 (21.0)	11 (52.4)	0 (0)
CD4+ T Cell Count	346 (187, 502.5)	361 (254, 551)	333 (150, 467)	400 (282, 640)	359 (240, 549)	236 (120, 456)
Undetectable HIV RNA (<150 c/mL)	16 (34.8)	3 (11.1)	8 (32.0)	3 (15.8)	8 (38.1)	0 (0)

RESULTS. CONTINUED

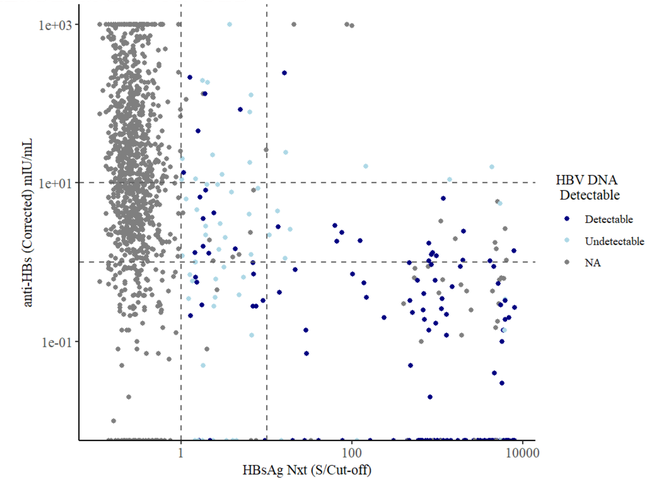


Figure 2. Within the HBsAg Nxt S/CO values of 1 to 10 and anti-HBs between 1 and 10, many participants (37%) had detectable HBV DNA. Individuals with detectable HBV DNA but had HBsAg Nxt < 10 may have been classified as negative by most commercially-available HBsAg assays.

Table 3. Associations with Detectable HBV DNA among PWID and MSM living with HIV and HBsAg Nxt Values between 1 and 10

	Undetectable HBV DNA (n=46)	Detectable HBV DNA (n=27)	OR (95% CI)	aOR (95% CI)
Median anti-HBs (mIUmL)	1.46 (IQR 0.35, 11.08)	1.29 (IQR 0.29, 6.67)	0.99 (0.99, 1.00)	0.99 (0.98, 1.00)
Median anti-HBc (S/CO)	0.535 (IQR 0.18, 4.34)	7.05 (IQR 4.89, 7.41)	1.47 (1.22, 1.78)*	1.57 (1.26, 1.95)*
CD4 < 200 (ref: >=200)	32 (59.3%)	22 (40.7%)	0.99 (0.97, 1.02)	0.99 (0.96, 1.04)
HIV Viral Suppression at Baseline (<150 c/mL)	16 (84.2%)	3 (15.8%)	0.23 (0.06, 0.90)*	1.05 (0.15, 7.47)
On ART at Baseline	21 (84.0%)	4 (16.0%)	0.21 (0.06, 0.69)*	0.10 (0.02, 0.64)*

*p<0.05

CONCLUSIONS

- Functional cure of HBV may not be binary but rather represents a continuum of the quantity of HBsAg in plasma
- Occult HBV (in which HBV DNA is detected in plasma without HBsAg) may actually represent low level expression of HBsAg

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ACKNOWLEDGEMENTS

We would like to thank our participants, without whom this research would not have been possible. This trial was supported by the National Institute on Drug Abuse of the National Institutes of Health (grant number: R01DA041034) and the Johns Hopkins Center for AIDS Research (grant number: P30 AI094189). C.L.T. is supported by R56AI138810. Abbott Laboratories donated kits for the characterization of HBV in this study as part of the Abbott Pandemic Defense Coalition. This research has been facilitated by the infrastructure and resources provided by the Johns Hopkins University Center for AIDS Research, an NIH funded program (1P30AI094189), which is supported by the following NIH Co-Funding and Participating Institutes and Centers: NIAID, NCI, NICHD, NHLBI, NIDA, NIA, NIGMS, NIDDK, NIMHD. T.A.L. is supported by the National Institutes of Health T32 Fellowship for HIV Epidemiology and Prevention Sciences (T32AI102623).