HBsAg SEROCLEARANCE IN HIV AND HBV-COINFECTED PATIENTS IN THE ERA OF TENOFOVIR-CONTAINING THERAPY

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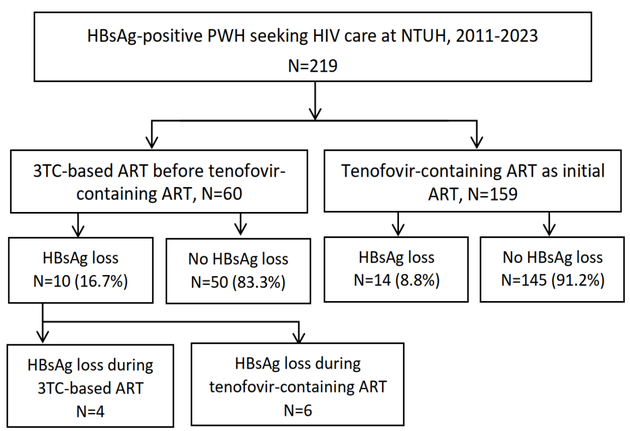
BACKGROUND

- HBsAg loss is considered functional cure and resolution of chronic HBV infection.
- Tenofovir is a nucleotide analog (NA) with potent anti-HBV activity, and long-term tenofovir-containing antiretroviral therapy (ART) can achieve durable HBV viral suppression in people with HIV/HBV coinfection. However, HBsAg and cccDNA levels are known to be minimally impacted by NA treatment.
- This study aims to investigate the incidence of and associated factors with HBsAg seroclearance after long-term tenofovir treatment in people with HIV/HBV coinfection.

METHODS

- People with HIV/HBV coinfection seeking HIV care and receiving tenofovir disoproxil fumarate (TDF)- or tenofovir alafenamide (TAF)-containing ART between 2011 and 2023 were included and followed until Dec. 31, 2024.
- Those with prior exposure to tenofovir or entecavir monotherapy for HBV or who had no follow-up HBsAg test were excluded.
- Data on demographics, plasma HIV RNA, CD4 count, liver function, serologic markers of viral hepatitis, plasma HBV DNA, and liver fibrosis stage were collected. Factors associated with HBsAg loss were analyzed using Cox proportional hazards model. Survival and liver outcomes were evaluated.

Figure 1. Study Flow



RESULTS

- 219 people with HIV/HBV coinfection were included; 60 of them received 3TC-based ART initially and switched to tenofovir-containing ART; and 16 (7.3%) were born in the era of nationwide neonatal HBV vaccination (after July 1986) (Table 1).
- At the end of follow-up, 24 (11%) of 219 PWH achieved HBsAg loss; 4 had HBsAg loss during 3TC-based ART and were excluded from the analysis of HBsAg seroclearance with tenofovir-containing ART (Fig 1).
- Kaplan–Meier estimates showed the cumulative incidence of HBsAg seroclearance was significantly higher in PWH born in HBV vaccination era and those with HBsAg ≤250 IU/mL at tenofovir initiation (Fig 2). In multivariable Cox regression analysis, born in HBV vaccination era (aHR 8.519), HBsAg ≤250 IU/mL at tenofovir initiation (aHR 4.822), and anti-HCV positivity at end of follow-up (aHR 5.586) were significantly associated with HBsAg seroclearance (Table 2).
- None of the PWH with HBsAg seroclearance developed cirrhosis or hepatocellular carcinoma (HCC), while 8.5% and 2.1% of PWH without HBsAg seroclearance developed cirrhosis and HCC, respectively (Table 3).

Table 1. Clinical characteristics of PWH with and those without HBsAg seroclearance at initiation of tenofovir (TFV)-containing therapy

Characteristics	No HBsAg seroclearance (n=195)	HBsAg seroclearance (n=20)	*p*
Age, median (IQR), years	37 (32-42)	37(29-45)	0.731
Born in HBV vaccination era (After July, 1986), n (%)	10 (5.1)	6 (30)	0.001
Male sex, n (%)	191 (97.9)	20 (100)	0.999
Risk group, n (%)			
Men who have sex with men	171 (87.7)	19(95)	0.332
People who inject drugs	7 (3.6)	1 (5.0)	0.751
Heterosexuals	14 (7.2)	0(0)	0.372
TFV-containing ART as initial regimen, n(%)	145 (74.4)	14 (70)	0.672
CD4, median (IQR), cells/μL	320 (109-503)	294 (147-525)	0.665
Plasma HIV RNA , log_{10}copies/mL	4.5 (1.8-5.1)	4.6 (1.6-5.2)	0.985
Plasma HBV DNA, log_{10} copies/mL	3.5 (6.1-2.9)	3.5 (2.1-5.4)	0.693
Plasma HBV DNA <20 IU/mL, n/n (%)	58/183 (31.7)	8/20 (40)	0.451
HBeAg-positive, n/n (%)	37/141 (26.2)	3/15 (20)	0.599
HBsAg ≤250 IU/mL, n/n (%)	43/188 (22.8)	12/19 (63.2)	<0.001
Anti-HCV-positive, n/n (%)	26/172 (15.1)	6/18 (33.3)	0.049
ALT, median (IQR), U/L	30 (22-58)	26 (21-44)	0.407
AST, median (IQR), U/L	32 (22-61)	29 (18-54)	0.367
Cirrhosis of the liver, n/n (%)	11/180 (5.5)	0/19 (0)	0.295

Figure 2. Kaplan-Meier estimates of the cumulative incidence of HBsAg seroclearance by (A) birth year in relation to neonatal HBV vaccination program and (B) baseline HBsAg level

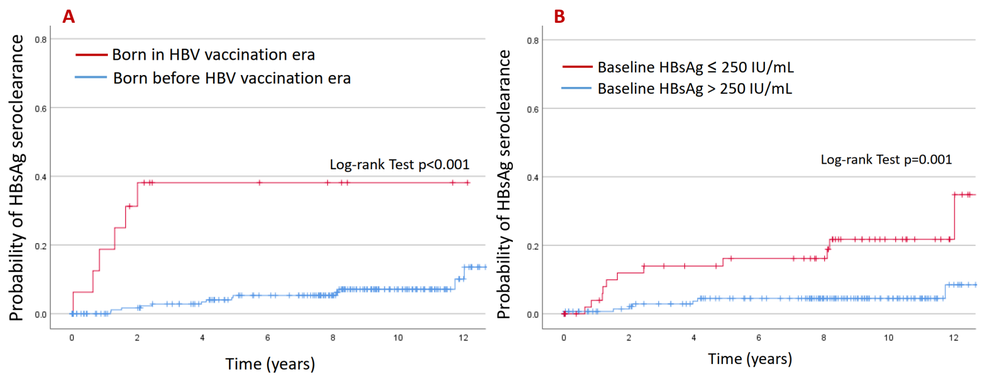


Table 2. Factors associated with HBsAg seroclearance

	Univariable		Multivariable	
	HR (95% CI)	*p*	aHR (95% CI)	*p*
Tenofovir-containing ART as initial ART regimen	1.540 (0.519-4.573)	0.437		
Born in HBV vaccination era	8.631 (3.245-22.960)	<0.001	8.519 (2.862-25.359)	<0.001
CD4 count at tenofovir initiation, per 1-cell/μlL increase	1.000 (0.998-1.002)	0.762		
HBV DNA ≤20 IU/mL at tenofovir initiation	1.017(.398-2.600)	0.972		
HBsAg ≤250 IU/mL at tenofovir initiation	4.600 (1.783-11.872)	0.002	4.822 (1.822-12.762)	0.002
Anti-HCV positivity at end of follow-up	5.588 (2.263-13.802)	<0.001	5.586 (2.100-14.860)	0.001

Table 3. Survival and liver outcomes

	No HBsAg seroclearance (n=195)	HBsAg seroclearance (n=20)	*P*
Death, n/n (%)	9 (4.6)	1 (5.0)	0.938
Liver-related death, n (%)	2 (1.0)	0 (0)	0.999
AST-to-platelet ratio index	0.32 (0.24-0.44)	0.27 (0.21-0.33)	0.114
Fibrosis-4 index	1.05 (0.72-1.37)	1.15 (0.84-1.72)	0.309
Cirrhosis of the liver, n/n (%)	16/189 (8.5)	0/19 (0)	0.187
Hepatocellular carcinoma, n (%)	4 (2.1)	0 (0)	0.999

CONCLUSIONS

- In the in era of tenofovir-containing ART, HBsAg seroclearance was uncommon in people with HIV/HBV coinfection.
- Lower baseline HBsAg level and HCV-coinfection were associated with HBsAg seroclearance in PWH receiving tenofovir-containing ART.
- The link between neonatal HBV vaccination and HBsAg loss suggests horizontal HBV transmission may lead to higher probability for HBsAg loss.