HBV Seroconversion in People With HIV: Relevance of Clinical History and Viral Markers Monitoring

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BACKGROUND

- Treatment including tenofovir disoproxil (TDF) or alafenamide (TAF) is the standard of care in people living with HIV/HBV coinfection.
- Serum HBV-RNA is an emerging biomarker reflecting the activity of intrahepatic HBV reservoir.

The aim of the study was to describe HBV seroconversion (HBV-S) rate in subjects with HIV/HBV coinfection on HBV-active therapy and to analyze markers of HBV activity after achieving HBsAg loss.

METHODS

Retrospective cohort study. **Inclusion criteria**:

- Individuals with HIV/HBV coinfection who attended the Modena HIV Clinic since 1985 onward.
- Two HBV serology measurements available
- Follow-up (FU) period of at least 6 months.

Data collection included: demographics and HIV history data (date of diagnosis, risk factor, AIDS diagnosis), HBV serological markers, presence of liver cirrhosis, liver transplantation, HDV and HCV serologies; Anti-HBV regimens with 3TC, TDF or TAF (at seroconversion and cumulative exposure).

HBV seroconversion (HBV-S) definition: detection of anti-HBs antibodies (HBsAb) at levels >10 UI/ml, simultaneously to the presence of HBsAg loss.

In a subset of individuals who experienced HBsAg loss, **Highly Sensitive (HS) HBV-DNA and HBV-RNA** Assays were quantified at last available FU (HS digital droplet PCR). The lower limit of quantification (LLOQ) of the technique was 1 IU/ml for HBV-DNA and 2 IU/ml for HBV-RNA.

Statistical Analysis performed after stratification according to HBV-S: analyses were conducted using univariate methods and logistic regression to identify factors associated with HBV-S.

A residual HBV activity may persist despite HBsAg loss during active HBV therapy: tenofovir discontinuation should be carefully evaluated and followed by proper monitoring of HBV markers.

RESULTS

163 subjects were included (Table1): **32 (20%) had HBsAg loss** and **19 (12%) had HBV-S**

HBV-S incident rate: 0.26 per 10,000 PYFU

Table 1. Population characteristics

	Total population (n=163)	Non HBV-S (n=144)	HBV-S (n=19)	p-value
Male gender, n (%)	125 (76.7)	112 (77.8)	13 (68.4)	0.365
Age at HIV diagnosis, years, median (IQR)	32 (25-40)	32 (25-40)	32 (24-34)	0.270
HIV risk factor, n (%)				0.841
Sexual	100 (61.3)	90 (62.5)	10 (52.6)	
Intravenous drug use	51 (31.3)	43 (29.8)	8 (42.1)	
Other	12 (7.4)	11 (7.7)	1 (5.3)	
Time from HBV diagnosis, years, median (IQR)	10 (5-19)	10 (5-18)	11 (7-17)	0.808
Time from HIV diagnosis, years, median (IQR)	16 (9-25)	16 (9-26)	16 (9-23)	0.942
HDV Ab, n (%)	12 (7.4)	12 (8.3)	0 (0)	0.214
HCV Ab, n (%)	55 (33.7)	43 (29.9)	12 (63.2)	0.004
AIDS diagnosis, n (%)	50 (30.7)	49 (34.0)	1 (5.3)	0.011
Cirrhosis, n (%)	28 (17.2)	25 (17.4)	3 (15.8)	0.864
Liver transplant, n (%)	4 (2.5)	2 (1.4)	2 (10.5)	0.016
Death, n (%)	35 (21.5)	34 (23.6)	1 (5.3)	0.067
ALT transaminase				
Baseline	26 (16-37)	28 (15-55)	20 (18-32)	0.726
Last determination	25 (18-39)	26 (18-41)	21 (15-27)	0.043
HBsAg Loss, n (%)	32 (19.6)	13 (9.0)	19 (100)	0.001
HBeAg Pos, n(%) (115 subj)	34 (29.6)	33 (32.7)	1 (7.1)	0.050
HbeAb Pos, n(%) (121 subj)	57 (47.1)	50 (47.6)	7 (43.7)	0.773
Anti-HBV at seroconversion or last available follow-up				0.013
3TC	38 (25.0)	32 (23.9)	6 (33.3)	
TDF	41 (27.0)	32 (23.9)	9 (50.0)	
TAF	73 (48.0)	70 (52.2)	3 (16.7)	
Anti-HBV Cumulative Exposure, months (number of exposed)				
3TC (110 subj)	54 (27-106)	54 (21-109)	61 (43-96)	0.519
TDF (126 subj)	55 (25-102)	52 (23-97)	75 (35-108)	0.215
TAF (80 subj)	50 (22-67)	50 (22-67)	66 (32-78)	0.480

Figure 1. HBV markers progression to seroconversion

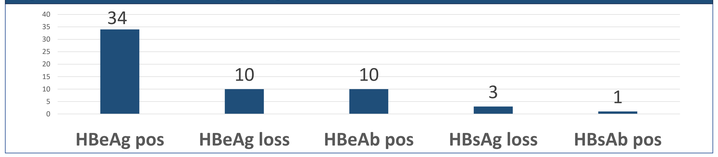


Figure 2. Highly Sensitive HBV-DNA and HBV-RNA Assays distribution

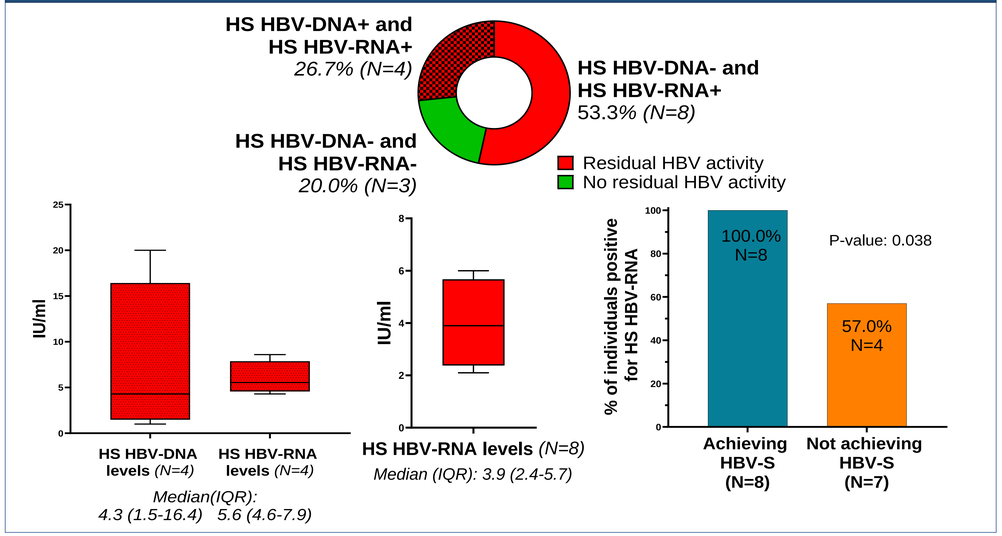


Table 2. Univariate and Multivariate Logistic Regression

	Univariate			Multivariate		
	OR	95%CI	p-value	aOR	95%CI	p-value
Positive HCV Ab, yes/no	4.03	1.48-10.92	0.006	6.4	2.2-19.1	0.001
AIDS history	0.11	0.01-0.83	0.033	0.1	0.01-0.61	0.016
Time from HIV diagnosis (Years)	0.99	0.95-1.04	0.813			
HbeAg at baseline (115 subj)	0.16	0.1-1.26	0.082			
Liver transplant, yes/no	8.35	1.10-63.19	0.040	8.4	0.92-77.14	0.060
Positive HBV RNA, yes/no	1.25	0.80-1.95	0.328			
Cumulative drug exposure (months)						
3TC	1.00	0.99-1.01	0.446			
TDF	1.00	0.99-1.00	0.373			
TAF	0.99	0.99-1.00	0.099			

CONCLUSIONS

- One out of 10 individuals with HIV/HBV co-infection in our cohort reached HBV seroconversion, in line with literature. Previous AIDS-related events did not favour seroconversion, while HCV co-infection seemed to be associated with the outcome.
- A residual HBV activity persisted despite HBsAg loss during active HBV therapy: tenofovir discontinuation should be carefully evaluated in those patients and, if pursued, a proper monitoring of HBV markers should not be missed.

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