Circulating HBV RNA Helps Characterize HBV Disease in Senegal

734

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Background

- Hepatitis B virus (HBV) infection affects >10% of the population in West Africa and is the most common cause of liver cirrhosis and hepatocellular carcinoma
- Circulating HBV RNA may help improve the characterization of HBV disease and prognosis.
- We aimed to evaluate the associations between circulating HBV RNA and conventional biomarkers of HBV replication in the Senegalese Hepatitis B Cohort study (SEN-B).

Methods

Study setting and population

- Cross-sectional analysis of treatment-naïve persons with HBV within SEN-B.
- SEN-B includes individuals aged >18 years with a positive hepatitis B surface antigen (HBsAg) test followed at the Infectious and Tropical Disease Service and the Ambulatory Treatment Center at Fann University Hospital, Dakar, Senegal.

Inclusion criteria

- We included all treatment-naïve participants without HIV infection who had a quantitative HBsAg (qHBsAg) >0.05 IU/ml and an HBV RNA measurement available at study inclusion.

Laboratory and definitions

- HBV RNA was measured using the cobas HBV RNA investigational assay (Roche Molecular Diagnostics, Pleasanton, CA) with a lower limit of detection <5 copies/ml and a lower limit of quantification of 10 copies/ml.
- Participants were classified into three phases of HBV infection: hepatitis e antigen (HBeAg)-positive (EP), HBeAg-negative chronic infection (ENCI) and HBeAg-negative chronic hepatitis (ENCH).
- ENCH was defined by HBV DNA ≥2000 IU/ml with elevated alanine aminotransferase (ALT ≥30 IU/ml for men, ≥19 IU/ml for women) and/or significant liver fibrosis (liver stiffness measurement >7.0 kPa).

Statistics

- We comapred participants with and without detectable HBV RNA using descriptive statistics.
- We evaluated associations between HBV RNA, HBV DNA and qHBsAg using Spearman's rank correlation coefficient among participants with detectable HBV RNA levels.

Results

Characteristics of the study population

- Of 918 participants included in SEN-B, we excluded 118 who had an HIV infection, 50 without a stored sample available prior to tenofovir start and 31 without qHBsAg >0.05 IU/ml.
- Of the remaining 719 participants, 17 (2.4%) were classified into the EP phase, 620 (86.2%) into the ENCI phase and 82 (11.4%) into the ENCH phase.
- Participants with detectable HBV RNA (358/719, 49.8%) had higher HBV DNA levels and were more likely to be HBeAg-positive and to have significant liver fibrosis than those with undetectable HBV RNA levels (**Table 1**).

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Main findings

Approximately 50% of treament-naïve persons with HBV in Senegal had detectable HBV RNA in the plasma.

Individuals with detectable HBV RNA levels had higher HBV DNA levels and were more likely to have significant liver fibrosis, as determined by transient elastography.

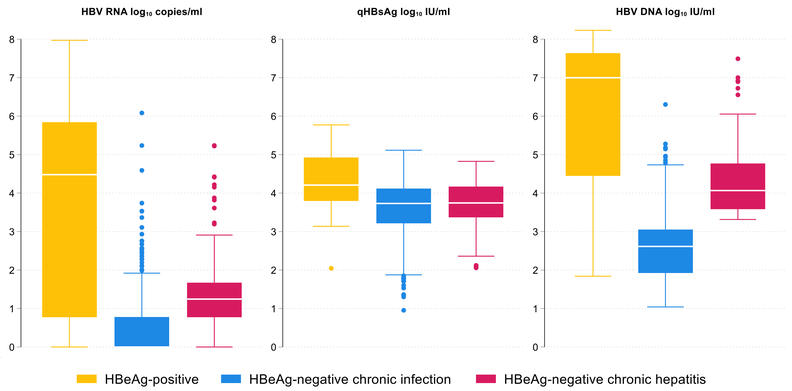
HBV DNA levels correlated well with HBV RNA in HBeAg-positive inviduals and those with HBeAg-negative chronic hepatitis, whereas qHBsAg levels only correlated with HBV RNA in HBeAg-positive individuals.

Table 1: Characteristics of participants, stratified by HBV RNA status

	Detectable HBV RNA N=358	Undetectable HBV RNA N=361	*p-value*
Age [years]	31.0 (25.0-37.0)	31.0 (25.0-39.0)	0.48
Female sex	161/358 (45.0%)	180/361 (49.9%)	0.19
BMI ≥30 kg/m²	21/352 (6.05%)	33/360 (9.1%)	0.11
Phase of HBV infection			<0.001
HBeAg-positive	14/358 (3.9%)	3/361 (0.8%)	
HBeAg-negative chronic infection	281/358 (78.5%)	339/361 (93.9%)	
HBeAg-negative chronic hepatitis	63/358 (17.6%)	19/361 (5.3%)	
qHBsAg level [IU/ml]	6,207 (2,128-14,580)	5,053 (1,632-12,920)	0.10
qHBsAg ≤1000 IU/ml	57/358 (15.9%)	71/361 (19.7%)	0.19
HBV DNA level [IU/ml]	1,375 (397-6,990)	271 (39-739)	<0.001
Hepatitis D antibody positive	0/358 (0.0%)	5/361 (1.4%)	0.03
Significant liver fibrosis (stiffness >7 kPa)	49/357 (13.7%)	27/361 (7.5%)	<0.01
Elevated ALT	104/358 (29.1%)	94/361 (26.0%)	0.37

Data are presented as median (IQR) for continuous measures, and n (%) for categorical measures. ***Abbreviations*** *ALT, alanine aminotransferase; BMI, body mass index; DNA; deoxyribonucleic acid; HBeAg, hepatitis B e antigen; HBV, hepatitis B virus; IU/ml, international units per milliliter; kPa, kiloPascal; qHBsAg, quantitative hepatitis B surface antigen; RNA, ribonucleic acid*

Figure 1: HBV RNA, qHBsAg and HBV DNA levels in the different phases of HBV infection



HBV RNA, HBV DNA and qHBsAg levels

- Lowest HBV RNA and HBV DNA levels were observed in the ENCI phase.
- qHBsAg levels did not differ between ENCI and ENCH phases, but were higher in HBeAg-positive participants compared to those in the ENCI and ENCH phase (**Figure 1**).

Figure 2: Correlation between HBV RNA and HBV DNA in the different phases of HBV infection

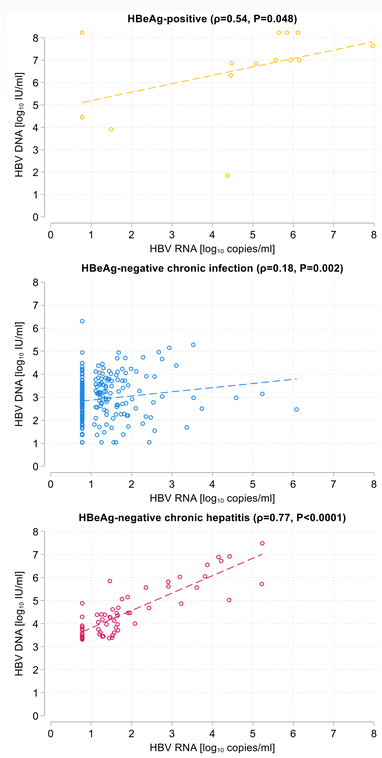
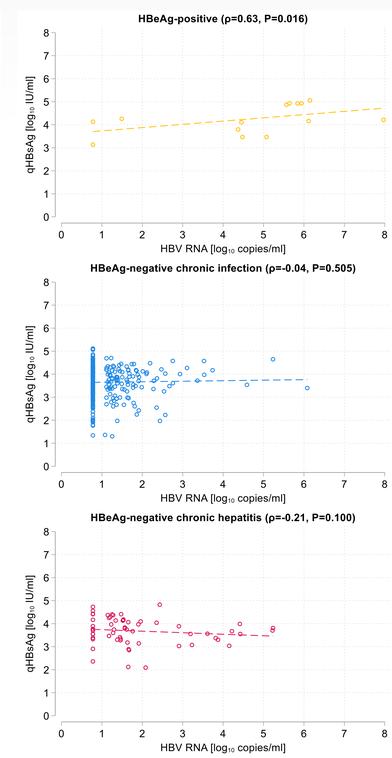


Figure 3: Correlation between HBV RNA and qHBsAg in the different phases of HBV infection



Correlation between HBV RNA, HBV DNA and qHBsAg

- HBV RNA correlated strongly with HBV DNA in ENCH, moderately in persons in EP and poorly in ENCI **(Figure 2)**
- HBV RNA correlated moderately with qHBsAg in EP, whereas no correlation was observed in HBeAg-negative individuals **(Figure 3)**

Conclusions

- HBV RNA levels differ between treatment-naïve persons with HBV from Senegal in the EP, ENCI and ENCH phases of HBV infection.
- Correlation of HBV RNA and HBV DNA depends on HBV infection phase with the strongest correlation observed in ENCH, whereas qHBsAg correlates with HBV RNA only in EP.
- HBV RNA may help characterize HBV infection phases and identify individuals with advanced liver fibrosis.

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