Hepatitis B RNA and core related antigen in HIV-HBV coinfection

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A joint venture between The University of Melbourne and The Royal Melbourne Hospital

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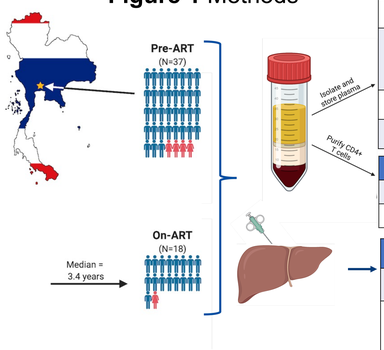
BACKGROUND

HBV core related antigen (HBcrAg) and HBV RNA are potential surrogate markers for intrahepatic HBV covalently closed-circular (ccc) DNA. cccDNA persists in infected hepatocytes despite HBV DNA suppression with antivirals. There are limited data on these markers in people with HIV-HBV co-infection on HBV-active antiviral therapy (ART).

METHODS

People with HIV-HBV co-infection naive to ART were recruited in Thailand in a prospective observational study. Liver fibrosis was measured by biopsy and transient elastography (TE) and blood and liver samples obtained pre- and following HBV-active ART.

Figure 1 Methods



Plasma	Method
HIV viral load	qPCR
HBV viral load	qPCR
Quantitative HBV surface antigen (qHBsAg)	Chemiluminescence
HBV crAg	Chemiluminescence
HBV RNA	Abbott m2000 PCR

CD4+ T cells	Method
Cell-associated HIV RNA	qPCR
Cell-associated HIV DNA	qPCR

HBV measurements	Method
Relaxed circular DNA (rcDNA)	qPCR
Covalently closed circular DNA (cccDNA) (n=27)	qPCR

Liver HBV cccDNA was quantified using droplet digital PCR. HBcrAg and HBV RNA were measured in plasma using a chemiluminescence assay and an in vitro PCR, respectively. Differences between groups were assessed by Mann-Whitney and correlations by calculation of Spearman's rank correlation coefficients.

RESULTS

Participants (n=37) were enrolled and followed for a median of 3.4 years of ART (n=18). They were mainly young men with median CD4+ T cell count pre- and on ART of 360 and 645 cells/μL respectively. At baseline, most had mild liver fibrosis (95% F0/F1 on biopsy) and the median (IQR) TE score was 6.2 (5.2, 8.1) kPa.

Following HBV-active ART in people living with HIV-HBV coinfection, there is no change in cccDNA or HBV RNA. On ART *both HBV RNA and core related antigen correlate with cccDNA including amongst HBeAg negative participants*, consistent with findings in HBV.

RESULTS (continued)

At baseline and on ART, 61% and 28% were HBeAg positive respectively. cccDNA was quantified in 22 participants at baseline, 11 of them also had follow-up results. HBcrAg and HBV RNA were quantified in 30 at baseline, 17 also had follow-up results.

	Baseline (pre-ART, n=37)	Follow up (on-ART, n=18)
Age, years (range) **Sex**, % female (n)	**31.9** (25.3-35.8) 10.3 (4/39)	**35.7** (24.8-47.5) 5.6 (1/18)
Duration on ART, median (range) **CD4 total**, cells/μL, median (range) **CD8 total**, cells/μL, median (range) **CD4/CD8 ratio**, median (range) **HIV RNA**, $\log_{10}$ copies/mL, median (range)	- **360** (221-462) **965** (662-1334) **0.37** (0.03-1.03) **4.9** (4.5-5.5)	**3.4** (2.0-4.1) **645** (281-1151) **844** (281-1451) **0.73** (0.21-1.43) **1.3** (1.3-1.6)
HBV DNA, $\log_{10}$ IU/mL, median (range) **HBeAg positive**, % (n)	**7.4** (2.6-8.1) **61.1** (22/36)	**1.0** (1.0-2.3) **27.9** (5/18)
Liver fibrosis **- Liver stiffness measurement- kPa (median, IQR)**	Mild **6.2** (5.2, 8.1)	Mild **5.2** (4.6, 7.7)

cccDNA, HBcrAg and HBV RNA were lower in HBeAg negative (pre ART n=6,8,8 respectively; on ART n=13) versus positive individuals (pre ART n=16,22,22 respectively; on ART n=5) both pre- and on ART ($p<0.005$ for comparisons) (Figure 2). Pairwise comparison of the same participants pre- and on ART showed no change in cccDNA (n=11) or HBV RNA (n=17) while HBcrAg decreased (n=17, p=0.034).

RESULTS (continued)

For all participants with available data pre-ART, both HBcrAg and HBV RNA correlated with cccDNA pre-ART (n=22; HBcrAg r=0.67, p=0.001; HBV RNA r=0.76, p<0.0001). Pre-ART HBV RNA correlated with cccDNA in eAg positive participants (n=16; r=0.54, p=0.041). cccDNA was negative in 5/6 eAg negative participants pre-ART (3 also had negative HBV RNA). For all participants on ART with available data both HBcrAg and HBV RNA correlated with cccDNA (n=17; HBcrAg r=0.81, p<0.0001; HBV RNA r=0.77, p=0.0002) and in the HBeAg negative subset (n=12; HBcrAg r=0.58, p=0.042; HBV RNA r=0.59, p=0.46) (Figure 3).

Figure 2 Pre- and on treatment cccDNA, HBV RNA and cccDNA

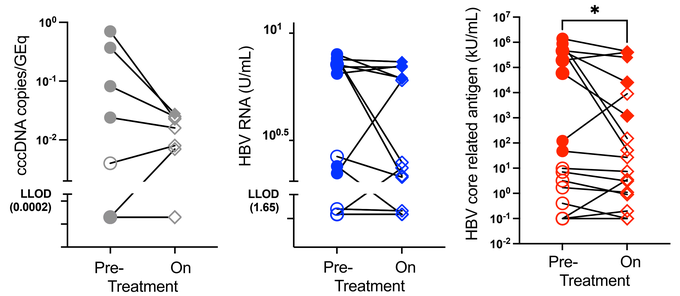
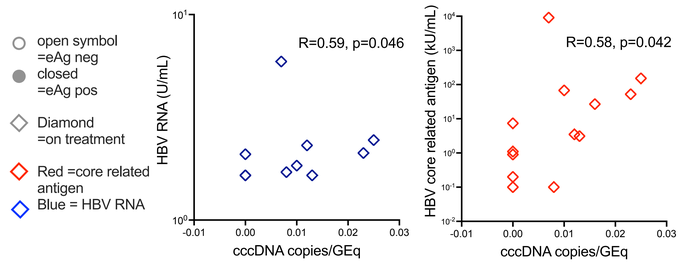


Figure 3 HBeAg negative on treatment HBV RNA and HBV crAg correlate with cccDNA



CONCLUSIONS

Following HBV-active ART in people living with HIV-HBV co-infection, there is no change in cccDNA or HBV RNA. On ART both HBV RNA and HBcrAg correlate with cccDNA including amongst HBeAg negative participants, consistent with findings in HBV monoinfection.

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Author 1 First Name Middle Initial Last Name[1], Author 2 First Name Middle Initial Last Name [2], Author 3 First Name Middle Initial Last Name [3] for the Research Group Name (**Bold presenting author's name**)
[1]Institution 1 Name, City, State (if US), Country, [2]Insittution 2 Name, City, Country, [3]Institution 3 Name, City, Country

BACKGROUND

- Clearly describe the hypothesis or research question addressed in the study. Why was the study conducted?

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METHODS

- Detail the experimental methods and processes employed in the study. What did you do?
- Collected [what] from [population]
- How you tested it.
- Illustrate your methods if you can!

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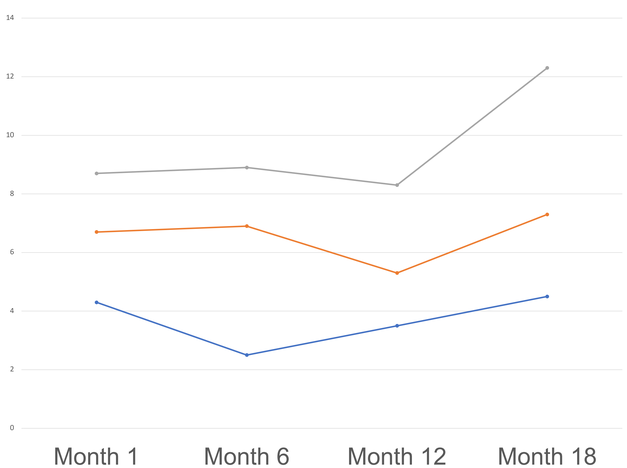

Place the main finding of your study in this shaded box to give attendees a quick understanding of the study. Emphasize important words with **bold** or *italic* font.

RESULTS

- Describe the precise findings of the study
- Describe what you found and **include data**
- Include tables, graphs, and figures

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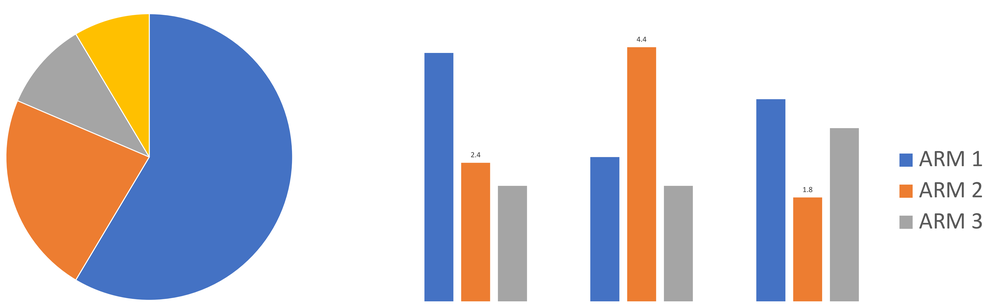

CONCLUSIONS

- Describe logically sound conclusions and reliable inferences drawn from the study results.
- Why are the study's findings important?

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