Characteristics and three year outcomes of antiviral-treated HIV, HBV and HIV/HBV co-infected patients in Tanzania

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Background

Hepatitis B virus (HBV) is a disease of global consequence, with 240 million chronic cases that result in over 780,000 chronic liver disease deaths each year. Chronic HBV infects >7% of individuals in Tanzania. An estimated 5-17% having HBV/HIV co-infection. Little is known about the long-term safety and efficacy of antiviral therapy in individuals HBV and HIV/HBV co-infection in this setting.

Objectives

To assess 12, 24- and 36-month month clinical, virologic and renal and liver outcomes in a cohort of HBV, HIV, and HBV/HIV co-infected subjects after initiation of antiviral therapy.

Methods

Study Design and Population: Subjects enrolled between 9/2013 and 4/2015 into a longitudinal cohort study of liver disease in HIV, HBV and HIV/HBV co-infection at Management and Development for Health (MDH) supported HIV and HBV clinics in Dar es Salaam, Tanzania were included in this study. Subjects were followed to 36 months at annual study visits, until 4/18.

Clinical Protocols: At each study visit, a comprehensive history and examination and study laboratory testing was performed. HIV mono-infected and HIV/HBV co-infected subjects received tenofovir, lamivudine, and efavirenz (TLE) at study entry. All HBV mono-infected subjects received lamivudine at enrollment and switched to tenofovir disoproxil fumarate (TDF) 1 to 2 years after enrollment when it became available in Tanzania. Laboratory testing included: hemoglobin, platelets, aspartate aminotransferase (AST), Alanine aminotransferase (ALT), creatinine (Roche Cobas Integra® 400+ Analyser), HBeAg/anti-HBe (EIA assay Cobas e411), HBV DNA (COBAS® Ampliprep Taqman 96, v2.0, Roche Diagnostics GmbH, Mannheim, Germany; lower limit of detection (LLD) of 20 IU/mL).

Outcome and Definitions: Liver fibrosis was measured using AST to Platelet Ratio Index (APRI). Creatinine clearance was determined using the 4-variable MDRD equation. Virologic suppression was defined as HBV DNA <20IU/mL, or HIV <20copies/mL, the lower limits of detection. Deaths were recorded after notification by family members, friends or the patient-tracking team. Causes of death were ascertained through medical records where available or a home-based health care report.

Statistical Analysis: Demographics were each described as proportions of the total cohort. Baseline characteristics were characterized using median values and interquartile ranges. APRI and eGFR at 12, 24, and 36-month follow-up visits were modelled using mixed effects models.

Results

Table 1. Baseline characteristics

Characteristic	All patients (n=502)	HIV/HBV co-infected (n=63)	HBV mono-infected (n=163)	HIV mono-infected (n=267)
Male (%)	219 (43.6)	31 (48.4)	109 (66.0)	79 (28.9)
Age, median (IQR)	36 (14)	36 (10)	38 (15)	32 (13)
BMI, median (IQR)	22.8 (6.6)	21.0 (5.9)	24.6 (6.4)	21.8 (6.9)
Platelets 10^9/L, median (IQR)	254.5 (130.0)	228.5 (113.0)	225.0 (64.0)	290.0 (143.0)
AST IU/L, median (IQR)	26.1 (12.7)	30.9 (24.0)	25.4 (11.1)	25.8 (11.4)
ALT IU/L, median (IQR)	19.1 (14.8)	20.1 (22.4)	22.2 (16.2)	16.6 (11.3)
CrCl, median (IQR)				
Baseline	115.1 (56.3)	119.6 (63.6)	98.6 (47.6)	124.2 (53.6)
Year 1	110.8 (52.8)	121.9 (76.5)	98.4 (36.6)	116.0 (64.7)
Year 2	112.8 (56.4)	122.9 (69.7)	98.8 (41.0)	123.7 (58.5)
Year 3	104.2 (43.8)	124.8 (39.2)	91.8 (29.0)	112.0 (45.1)
APRI, median (IQR)				
Baseline	0.27 (0.20)	0.32 (0.34)	0.29 (0.16)	0.23 (0.18)
Year 1	0.26 (0.20)	0.25 (0.25)	0.31 (0.21)	0.25 (.18)
Year 2	0.26 (0.18)	0.24 (0.12)	0.30 (0.18)	0.24 (0.15)
Year 3	0.26 (0.20)	0.26 (0.13)	0.29 (0.22)	0.23 (0.19)
HIV suppressed (<LLD) (%)				
Baseline	52 (22.9)	18 (28.5)	34 (20.7)	
Year 1	138 (78.9)	34 (77.3)	104 (79.4)	
Year 2	120 (82.8)	28 (82.4)	92 (82.9)	
Year 3	107 (89.2)	17 (100.0)	90 (87.4)	
CD4 (median (IQR)), baseline	213.0 (229.0)	238.0 (287.0)		209.0 (212.0)
HBV suppressed (<LLD) (%)				
Baseline	4 (0.5)	3 (5.2)		1 (0.4)
Year 1	156 (64.5)	34 (75.6)		122 (62.0)

Figure 1. Changes in APRI over time, by group

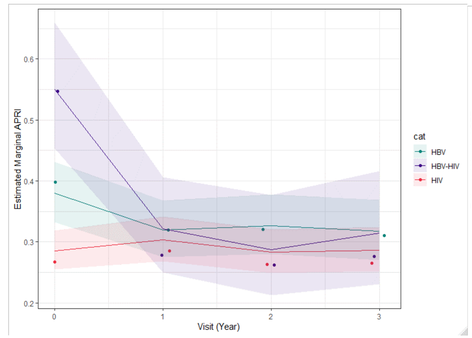
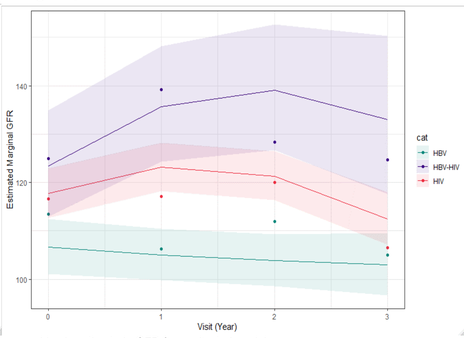


Figure 2. Changes in eGFR over time, by group



Line is estimated eGFR from adjusted model
Dots are observed mean eGFR per group per visit

- Declines in APRI were only significant from baseline to year 1 HIV/HBV co-infected subjects and from year 1-3 in HBV mono-infected; no significant changes were observed in HIV mono-infected subjects throughout follow up.
- Lower baseline APRI, older age, male sex, and alcohol use were significantly associated with lower odds of a ≥30% decline in APRI during follow-up in multivariable analyses (p's<.01).
- Unadjusted eGFR models showed a significant decline in eGFR in HBV mono-infected subjects (p = 0.01) and significant increase in HBV/HIV co-infected (p = 0.005) subjects. No significant changes in eGFR were observed in HIV mono-infected subjects.
- During the study period, 47 (9.4%) subjects died [HIV/HBV 13 (20.0%), HBV 4 (2.5%), HIV 30 (11.1 %)], with deaths significantly higher in HIV mono and co-infected patients as compared to HBV mono-infected patients (p = <0.001).
- Almost all deaths in HIV and HIV/HBV co-infected occurred within the first year of follow up and were due to OIs. All 4 deaths in the HBV group were liver-related.

Conclusions

- In this Tanzanian cohort, antiviral therapy was associated with high rates of virologic suppression and improvement in APRI score among JHIV, HBV mono-infected and HIV/HBV co-infected subjects
- HBV co-infection was not associated with worse liver outcomes during follow up in HIV-infected individuals
- Most of the higher mortality observed in HIV mono and co-infected patients was HIV-related and occurred early, whereas all HBV deaths were liver-related
- Significant declines in eGFR were observed in HBV mono-infected subjects. Further work is needed to examine the effects of switching to TDF on these declines.

Acknowledgements

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References

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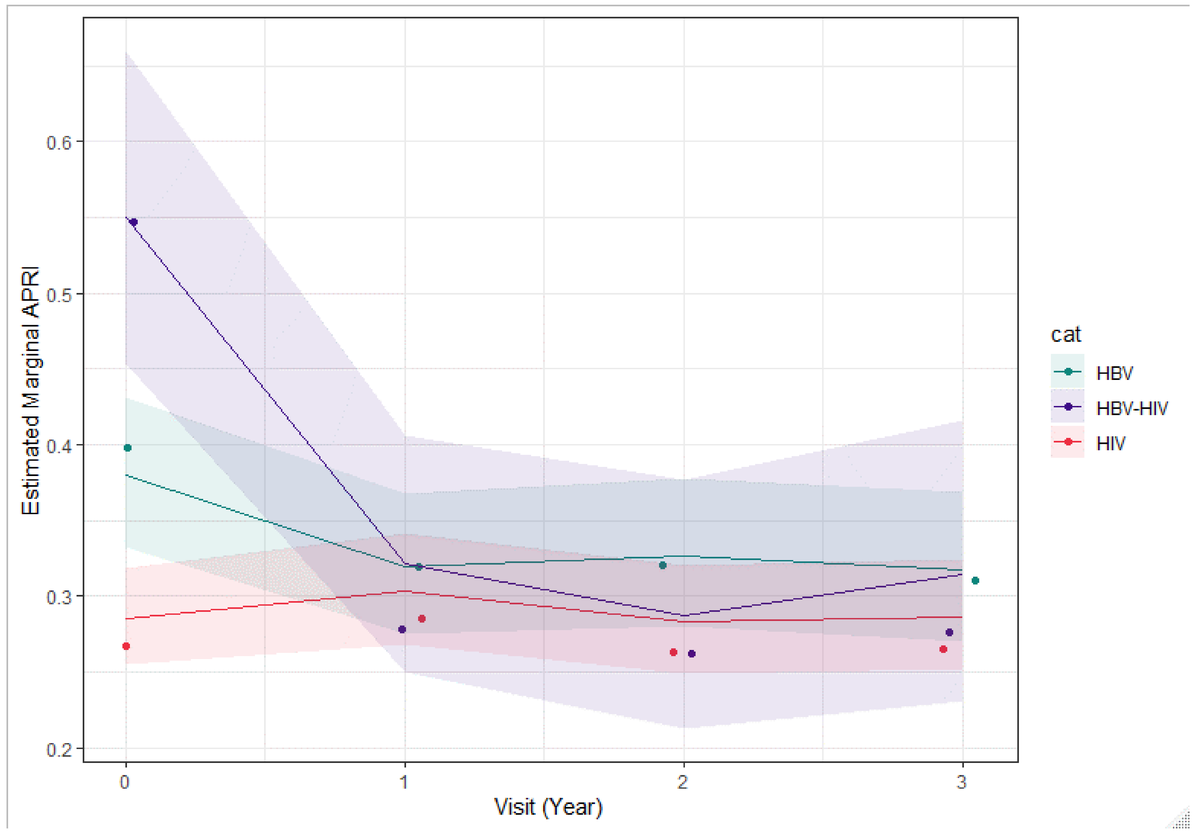

This is the APRI figure. I think we can include it in the poster. There's significant decline in the co-infected group starting at Year 1 then plateaud.

For HBV mono, significant decline only occurred in visit 3

HIV mono did not significantly change over time.