Incidence and risk factors for hepatitis B in HIV-infected adults in Rakai, Uganda

E Seremba[1], V Ssempijja[2], S Kalibbala[3], R Gray[4], M Wawer[4], F Nalugoda[3], C Casper[5], P Ocama[1], D Serwadda[1], DL Thomas[7], SJ Reynolds[6,7]

[1]Makerere University College of Health Sciences, Kampala, Uganda, [2]Clinical Research Directorate/Clinical Monitoring Research Program, Leidos Biomedical Research, Inc., Frederick National Laboratory for Cancer Research, Frederick, Maryland 21702, [3]Rakai Health Sciences Program, Kalisizo, Uganda, [4]Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, [5]Fred Hutchinson Cancer Research Center and University of Washington, Seattle, WA, [6]Division of Intramural Research, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, MD, [7]Johns Hopkins University School of Medicine

Background:

- Co-infection with Hepatitis B (HBV) and HIV is common in sub-Saharan Africa (SSA) and accelerates progression of liver disease to cirrhosis and other complications.
- Vaccination of HIV-infected adults for HBV is standard of care in developed countries but not yet policy in SSA where HBV is believed to be acquired in childhood and where there is a lack of HBV incidence data.
- We investigated the incidence and risk factors associated with HBV among HIV infected adults in Rakai, Uganda.

Methods:

- We screened stored sera from HIV-infected adults aged 15-49 years enrolled in the Rakai Community Cohort Study, an open cohort that conducts survey rounds every 1-1/2 years in which sociodemographic and clinical data, and sera are collected with the purpose of monitoring HIV trends in rural Southwestern Uganda.
- We tested 944 samples (collected between September 2003 and March 2015) for evidence of exposure to HBV using the hepatitis B core antibody (anti-HBc) marker.
- Serum from participants who tested anti-HBc negative (497) at the baseline round was tested over 3-7 consecutive survey rounds for either anti-HBc or hepatitis B surface antigen (HBsAg) sero-conversion.
- Exact poisson incidence methods were used to estimate the incidence of HBV with 95% confidence intervals while the Cox proportional regression methods were used to estimate adjusted hazard ratios of ART use and other confounders.

Results:

- 39 infections occurred (8 positive for both HBsAg and anti-HBc, 3 for HBsAg only and 28 for anti-HBc only) over 3,342 person years (pys), incidence of 1.17/100 pys.
- HBV incidence was significantly lower with ART use: 0.48 /100 pys with ART and 2.34/100 pys without ART (p<0.001) and significantly decreased with age: 2.60/100 pys if 15-29 years, 1.32/100 pys if 30-39 years and 0.48/100 pys if 40-50 years (p<0.001).
- Adjusted hazard ratios of HBV incidence significantly differed by ART use: non ART use versus ART use, aHR=0. 33(95% CI=0.2-0.6), lamivudine (3TC) use: no ART versus 3TC-based ART, aHR= 0.24(0.1-0.5), p=<0.001) and by age: 40-50 years versus 15-29 years, aHR= 3.66(1.3-10.2); 40-50 years versus 30-39 years, aHR=2.18(0.9-5.4).

Results:

Figure 1: participant selection

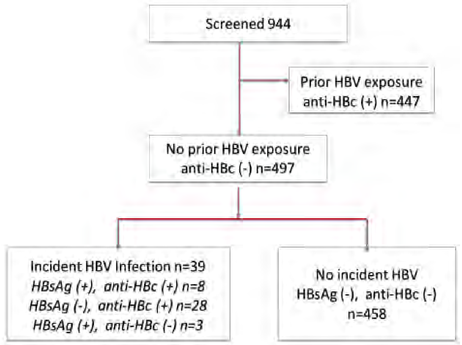

Table 1: Baseline characteristics.

Characteristic	N (%)
Gender	
Female	354(71%)
Male	143(29%)
Median age (IQR) years	30(IQR=25-34)
Age categories	
40+	50(10%)
30-39	208(42%)
15-29	239(48%)
Median CD4 count	464(IQR=291-674
Sexual partners in last year	
0	58(12%)
1	348(70%)
≥2	91(18%)

Table 2: Factors associated with incident hepatitis B disease

Characteristics	Cases/ person years	Incidence/ 100 person years	Unadjusted HRs 95% CI	Unadjusted HRs p-value	Adjusted HRs 95% CI	Adjusted HRs p-value
Overall	39/3342	1.17				
Gender						
Female	30/2380	1.26	Ref		Ref	
Male	9/962	0.94	0.74 (0.4-1.6)	0.43	0.86 (0.4-1.8)	0.70
Age						
40+	6/1256	0.48	Ref		Ref	
30-39	22/1662	1.32	2.78 (1.1-6.9)	0.004	2.18 (0.9-5.4)	
15-29	15/423	2.60	5.46 (2.0-14.8)		3.66 (1.3-10.2)	0.05
On ART*						
No	29/1238	2.34	Ref		Ref	
Yes	10/2103	0.48	0.20 (0.1-0.4)	<0.001	0.24 (0.1-0.5)	<0.001
Sex partners in last year						
0	8/813	0.98	Ref			
1	25/2089	1.20	1.21(0.5-2.7)	0.83		
>=2	6/440	1.36	1.38 (0.5-4.0)			
CD4 Count**						
0-99	1/55	1.81	Ref			
100-250	3/213	1.41	0.77 (0.1-7.4)	0.97		
251-499	12/740	1.62	0.89 (0.1-6.9)			
500+	12/903	1.33	0.74 (0.1-5.7)			

* Overall 287/497 initiated ART. At baseline, only 22 were on ART. Majority started ART in the observation period.
**CD4 test results were available for only 313 persons

Table 3: Association of ART regimen type with incident hepatitis B

Characteristics	HBV incidence: Cases/person years (pys)	HBV incidence: Incidence/100 pys (95% CI)	Unadjusted HRs 95% CI	Unadjusted HRs p-value	Adjusted HRs 95% CI	Adjusted HRs p-value
ART regimen						
No ART	29/1241	2.58(1.82-3.65)	Ref		Ref	
3TC	7/1243	0.89(0.49-1.60)	0.24(0.10-0.54)	0.001	0.29(0.13-0.69)	0.005
3TC and TDF	0/223	-	-	-	-	-
None 3TC/TDF	0/3.4	-	-	-	-	-

Study outcomes

- Thirty-nine new infections occurred over a period of 3,342 person years resulting in an incidence of 1.2 per 100 person years
- Overall, ART use was associated with a 76% reduction in incident HBV infection.
- No new HBV infection occurred among individuals that were on a tenofovir based ART regimen.
- Young adulthood (15-29 years) was associated with a high risk of incident HBV disease

Limitations

- Convenience sample was used
- Some missing data

Conclusions

- HBV transmission occurs in adults in a country where this disease was thought to be primarily transmitted in childhood suggesting need for vaccine preventive strategies
- Our findings add to the growing body of knowledge that suggests that HBV active medications in an ART regimen offer prophylaxis against incident HBV.

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•**Contact:** Emmanuel Seremba, MBChB, MMED, Makerere University College of Health Sciences, email: eseremba@gmail.com

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