MORTALITY OF HIV/HBV COINFECTED PATIENTS ON ART IN URBAN AND RURAL SOUTHERN AFRICA

Jonas Hector
SolidarMed
Ancuabe, Mozambique
j.hector@solidarmed.ch

Jonas Hector[1], Michael J Vinikoor[2,3], Kalo Musukuma[2], Roma Chilengi[2], Laura Jefferys[1], Michael Hobbins[1], Mary-Ann Davies[4], Matthias Egger[4,5], Gilles Wandeler[5,6]
for IeDEA-Southern Africa

[1] SolidarMed, Ancuabe, Mozambique, [2] Centre for Infectious Disease Research in Zambia, Lusaka, Zambia, [3] Department of Medicine at University of Alabama, Birmingham, United States of America, [4]School of Public Health and Family Medicine, University of Cape Town, Cape Town, South Africa [5]Institute of Social & Preventive Medicine (ISPM), University of Bern, Switzerland; [6]Department of Infectious Diseases, Bern University Hospital, University of Bern, Switzerland

Background

- Chronic hepatitis B virus (HBV) infection affects approximately 10% of HIV-positive people in sub-Saharan Africa (SSA)[1] and is an important risk factor for liver-related events and death.
- Due to high rates of losses to follow-up (LTFU) in African HIV clinics[2], precise mortality estimates among cohorts of patients on antiretroviral therapy (ART) are scarce.

Objectives

- To compare one-year mortality of HIV/HBV-coinfected patients on tenofovir (TDF)-containing ART between rural and urban primary care clinics in southern Africa after the systematic tracing of patients LTFU.
- To assess risk factors for all cause mortality.

Methods

Study Population and Inclusion Criteria

- We included HIV/HBV coinfected adults (>16 years) initiating TDF-containing ART at two urban clinics in Lusaka, Zambia, and three rural clinics in northern Mozambique between May 2013 and July 2015.

Procedures

- HBV infection was assessed using HBsAg rapid tests (Determine®).
- Quantitative real-time PCR for HBV viral load was performed using the COBAS Ampliprep/TaqMan System and HBV sequencing according to an in-house protocol[1].
- Medication possession ratio (MPR, calculated as days of ART possession/ 365 days*100) was used as a proxy for treatment adherence[3].
- All patients LTFU (>3 months without a clinical visit) were traced by phone and home visits for ascertainment of vital status.

Statistical analyses

- Baseline characteristics were compared between treatment settings using Fisher`s exact test and Wilcoxon rank sum tests.
- Mortality and associated risk factors were assessed using multivariable Cox proportional hazards regression.

Results

Table 1. Demographic and clinical characteristics, by country

	Rural Mozambique	Urban Zambia	p-value
	N=78	N=184	
Female (%)	47 (60.3)	76 (41.3)	<0.001
Median age in years (IQR)	30 (25-39)	34 (28-39)	0.14
Median BMI (IQR)	19.5 (18.2- 21.6)	20.2 (18.6-23.1)	0.11
Median CD4 cells/µl (IQR)	232 (122-539)	208 (97-351)	0.03
WHO stage 3 or 4 (%)	33 (42.3)	74 (41.6)	0.50
Median ALT (IQR)	31 (19-59)	23 (15-40)	0.04
Moderate to severe anemia (%)	34 (56.7)	43 (25.3)	<0.001
HBV genotype (%)			<0.001
A1	68 ()	41 ()	
E	14 ()	50 ()	
Other			
HBV viral load >20,000UI/ml (%)	38 (52.8)	77 (45)	0.17

- 263 HIV/HBV-coinfected patients were included. Patients in Mozambique were more likely to be female, to have moderate or severe anaemia (<11g/dl for men and < 10g/dl for women), elevated ALT levels and higher CD4 cell counts (Table 1).
- At 1 year, after the systematic tracing of patients LTFU, vital status was unknown in only one patient (1.3%) in Mozambique and 7 patients (3.8%) in Zambia.
- The MPR in patients with one year follow up was 69% (95% CI 20.3-89.3) in Mozambique and 97% (95% CI 97.8-100) in Zambia (p<0.01).

Figure 1. Survival of HIV/Hepatitis B-coinfected patients on ART, by country

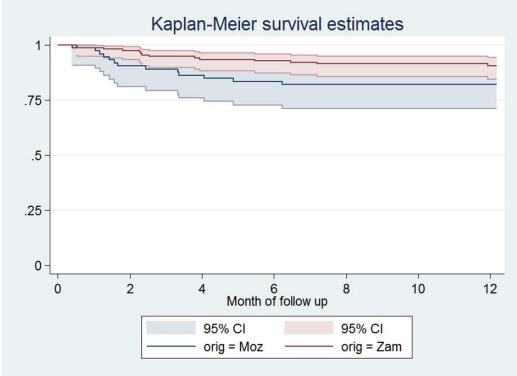

Table 2. Risk factors for mortality

	HR (95% CI)	P-value	aHR (95% CI)	p-value
Origin (ref: Moz)	0.49 (0.23-1.04)	0.06	1.56 (0.51-4.81)	0.43
Male sex	3.36 (1.36-8.35)	0.01	4.00 (1.07-15.01)	0.04
Moderate/severe anemia	6.50 (2.58-16.38)	<0.001	8.64 (2.35-31.78)	0.001
CD4<200/µl	2.22 (0.94-5.23)	0.07	0.84 (0.29-2.49)	0.76
Age in years	1.04 (1.00-1.07)	0.05	1.01 (0.97-1.07)	0.52
BMI	0.75 (0.64-0.88)	<0.001	0.72 (0.57-0.91)	0.01
HBV Viral load > 20,000 IU/ml	0.96 (0.42-2.23)	0.93	-	-
ALT	1.00 (0.98-1.01)	0.61	-	-
WHO stage 3 or 4	2.06 (0.96-4.45)	0.06	0.82 (0.30-2.31)	0.72

HR: hazard ratios, aHR: adjusted hazard ratios, CI: confidence interval, BMI: body mass index, ALT: alanine aminotransferase

- One-year mortality was 16 % in Mozambique and 8% in Zambia (p=0.06) (Fig. 1).
- In adjusted analyses, low BMI, moderate/severe anaemia and male sex were independent risk factors for mortality (Table 2).
- HBV viral load did not have an impact on 1-year mortality among HIV/HBV-coinfected individuals on TDF-containing ART.

Conclusions

- Early mortality of HIV/HBV-coinfected individuals on ART is very high in SSA, especially in rural settings, where access to care and treatment adherence may be reduced.
- Tracing of patients LTFU is needed if precise mortality estimates are to be obtained in rural SSA clinics.

References
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