



Hepatitis B infection in people living with HIV who initiate antiretroviral therapy in Zimbabwe

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Setting: There is little information about the diagnosis and treatment of hepatitis B virus (HBV) infection in people living with HIV (PLHIV) in Zimbabwe despite recommendations that tenofovir (TDF) + lamivudine (3TC) is the most effective nucleoside/nucleotide reverse transcriptase inhibitor (NRTI) backbone of antiretroviral therapy (ART) in those with dual infection.

Objective: To determine 1) numbers screened for hepatitis B surface antigen (HBsAg); 2) numbers diagnosed HBsAg-positive along with baseline characteristics; and 3) NRTI backbones used among PLHIV initiating first-line ART at Mpilo Opportunistic Infections Clinic, Bulawayo, Zimbabwe, between October 2017 and April 2019.

Design: This was a cross-sectional study using routinely collected data.

Results: Of the 422 PLHIV initiating first-line ART (median age 34 years, IQR 25–43), 361 (85%) were screened for HBV, with 10% being HBsAg-positive. HBsAg positivity was significantly associated with anaemia (adjusted prevalence ratio [aPR] 2.3, 95%CI 1.1–4.7) and elevated alanine transaminase levels (aPR 2.9, 95%CI 1.5–5.8). Of 38 PLHIV who were diagnosed HBsAg-positive, 30 (79%) were started on ART based on tenofovir (TDF) and lamivudine (3TC), seven were given abacavir (ABC) + 3TC-based ART and one was given zidovudine (ZDV) + 3TC-based ART.

Conclusion: In PLHIV, HBV screening worked well, the prevalence of HIV-HBV co-infection was high and most patients received appropriate treatment for both conditions. Recommendations to improve screening, diagnosis and treatment of HIV-HBV co-infection are discussed.

Chronic hepatitis B virus (HBV) infection is a major public health challenge worldwide, with 250 million people estimated to be hepatitis B surface antigen (HBsAg) positive.¹ The highest HBV infection rates are in sub-Saharan Africa and the Western Pacific, where transmission occurs predominantly in infants and children by perinatal and horizontal routes through close contact with family members.^{1,2} The outcome of HBV infection is age-dependent, with 95% of neonates, 20–30% of children aged 1–5 years and <5% of adults developing chronic infection.¹ There is considerable morbidity and mortality associated with chronic infection. Approximately 25% of people who acquire HBV in infancy or childhood develop cirrhosis or liver cancer.³ Various factors increase this risk of liver disease, one being advanced immunosuppression as a result of HIV co-infection.^{4–6}

There is considerable overlap between HIV infection and HBV. The global HIV-HBV co-infection prevalence is estimated at about 6% among people living with HIV (PLHIV), with the greatest burden of dual disease being in sub-Saharan Africa.⁷ This is supported by studies from Mozambique, Benin, Ghana and Ethiopia showing considerably higher rates of HBV among PLHIV.^{8–11} While HIV hastens the progression of HBV to cirrhosis and liver cancer,^{4–6} HBV, in turn, adversely affects the treatment of HIV and is associated with poor viral suppression, inadequate CD4 cell recovery and continued immune suppression despite antiretroviral therapy (ART).¹²

There are oral antiviral drugs available to treat both infections, suppress viral replication, and in the case of HBV, reduce hepatic inflammation and prevent progression to cirrhosis and liver cancer. Lamivudine (3TC) and tenofovir (TDF) are respectively the nucleoside/nucleotide reverse transcriptase inhibitors (NRTI) used to treat both HIV and HBV infections. TDF (in the prodrug form of either tenofovir disoproxil fumarate or tenofovir alafenamide) is the recommended first-line treatment for HBV because of its high barrier to resistance: 3TC is effective, but resistance can develop rapidly, especially with monotherapy.² None of these drugs can eradicate HIV or HBV and long-term treatment is therefore required to maintain viral suppression.

The National AIDS Programme in Zimbabwe has a well-performing HIV care and treatment programme, with over one million PLHIV alive and on ART.¹³ Two studies from Zimbabwe collecting blood samples between 2003 and 2014 in the largely pre-ART era showed that 11–17% of PLHIV had HBV co-infection as determined using HBsAg testing.^{14,15} More up to date and comprehensive information about HBV co-infection in PLHIV who are taking ART is needed. The 2016 national ART guidelines, which are in line with WHO guidelines, recommend TDF + 3TC as the NRTI backbone in PLHIV starting ART for the first time (Table 1).^{16,17} This regimen is ideal for those also infected with HBV. However, sometimes adults and adolescents are started on a zidovudine (ZDV) + 3TC backbone and children may be given abacavir (ABC) instead of TDF (Table 1). In the routine setting, the National AIDS Programme is interested to know the proportion of PLHIV given TDF + 3TC and which NRTI backbone is being used among the remainder.

We therefore aimed to document the prevalence and associated risk factors of HBV co-infection among PLHIV starting first-line ART, as well as the NRTI back-

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bones used in the ART regimens. Specific objectives were to determine 1) numbers screened for HBsAg; 2) numbers diagnosed HBsAg-positive, along with baseline demographic and clinical characteristics; and 3) the NRTI backbone used in the first-line ART regimen among PLHIV initiating first-line treatment at the Mpilo Opportunistic Infections (OI) Clinic, Bulawayo, Zimbabwe, between October 2017 and April 2019.

METHOD

Study design

This was a cross-sectional study using secondary data.

Setting

General setting

Zimbabwe is a low-income country in southern Africa with a population of about 13 million and a gross domestic product per capita of US\$924.^{18,19} HIV remains a major health challenge, with an estimated 1.3 million PLHIV at the end of 2016.¹³ By 2017, about one million out of the 1.3 million PLHIV had access to ART, up from just 12 000 in 2005.¹³ The country is making good progress towards the attainment of the UNAIDS 90-90-90 targets, with 74% of PLHIV knowing their HIV status, 87% of those diagnosed with HIV on ART and 87% of those on ART being virally suppressed.¹³

Specific setting and management of HIV and ART

Mpilo OI Clinic in Bulawayo was a pioneering and referral centre of excellence in ART roll-out in the public sector in Zimbabwe in 2004. With 11 500 PLHIV registered clients by the end of 2018, the centre is considered a high-volume ART facility. All PLHIV initiated on ART are registered in the ART register. An electronic patient record file has also been opened using national 'ePOC' software, which serves as the primary data source and is updated at every patient visit. After starting first-line ART, PLHIV are seen initially monthly and then 3-monthly for follow-up visits.

HBV screening in PLHIV and subsequent management at Mpilo Clinic

HBV screening at Mpilo OI commenced in October 2017. All PLHIV newly initiating first-line ART are prioritised and HBV screening is done within 1 month of initiating treatment. Whole blood is collected and

screened for HBsAg (OnSite HBsAg Rapid test, CTK Biotech Inc, CA, USA) at the laboratory located within the OI clinic. The results are entered into the paper-based laboratory register and the laboratory request form. The latter goes to the data clerk for entry into the ePOC file. For patients diagnosed with HIV-HBV coinfection, an abdominal ultrasound is carried out after the diagnosis has been made and a full set of liver function tests are performed every 3 months. If any of these tests are abnormal, the patients are referred to medical specialists for further management.

Study population

The study population included all PLHIV aged ≥ 5 years who initiated first-line ART at Mpilo OI Clinic between October 2017 and April 2019. PLHIV who were referred or transferred in from another HIV clinic were excluded.

Data variables, source of data and data collection

Data variables included patient ID Number, whether screened for HBV infection (yes/no), HBsAg result (positive/negative), ART regimen used, age, sex, marital status, employment, height, weight, CD4 cell count, creatinine clearance (ml/min), haemoglobin (g/dl) and alanine transaminase level (ALT in U/L). Males with haemoglobin <13 g/dl and females with haemoglobin <12 g/dl were classified as anaemic.²⁰ Body mass index (BMI) was calculated in kg/m². The data source for the study variables was the 'ePOC' database.

Analysis and statistics

Anonymised data were exported to MS Excel (Microsoft, Redmond, WA, USA) for cleaning and formatting. After cleaning, the database was imported into EpiData Analysis 3.1 (EpiData Association, Odense, Denmark) and Stata v12 (StataCorp, College Station, TX, USA) for analysis. Categorical variables were summarised using frequencies and proportions; continuous variables were summarised using means and standard deviations or medians and interquartile ranges (IQRs). Key outcome variables were HBV screening and HBV co-infection. Factors associated with HBV co-infection were analysed using the χ^2 test and presented as prevalence ratios (PR) with 95% confidence intervals (CIs). Modified Poisson re-

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TABLE 1 First-line ART regimens used in Mpilo Clinic, Bulawayo, Zimbabwe

	Adults and adolescents			Children	
	Preferred first-line ART	Alternative first-line ART		Preferred first-line ART	Alternative first-line ART
Adolescents (10–19 years) ≥ 35 kg	TDF+3TC+EFV	TDF+3TC+NVP	0–2 weeks	ZDV+3TC+NVP	
Adults, pregnant and breastfeeding women		ZDV+3TC+EFV ZDV+3TC+NVP	2 weeks to <3 years	ABC+3TC+LPV/r	ZDV+ 3TC+ LPV/r ABC+ 3TC+NVP
TB-HIV; HBV-HIV			3 years to <10 years	ABC+3TC+EFV	ZDV+3TC+EFV ZDV+3TC+NVP TDF+3TC+EFV (NVP)

gression was used with robust variance estimates to calculate adjusted prevalence ratios (aPRs) and 95% CIs. Levels of significance were set at 5%.

Ethics

Permission for the study was obtained from the Mpilo Institutional Ethics Review Board, Bulawayo, Zimbabwe. Ethics approval was obtained from the Medical Research Council of Zimbabwe, Harare, Zimbabwe (MRCZ/E/253); and the International Union Against Tuberculosis and Lung Disease Ethics Advisory Group, Paris, France (no 41/19). As the study involved only records review, requirement for informed consent was waived.

RESULTS

Of the 422 PLHIV (median age 34 years, IQR 25–43) who initiated first-line ART, 361 (85.5%) were screened for HBV infection (Table 2). Demographic and clinical characteristics were similar between those screened and not screened (data not shown). The proportions screened for HBV were highest in the youngest age groups and declined in the older age groups, but there were no other differences with respect to other baseline characteristics.

The proportion of PLHIV who were HBsAg-positive among those screened was 10.5% (95%CI 7.8–14.1). Baseline characteristics associated with being HBsAg-positive are shown in Table 3.

TABLE 2 Characteristics of PLHIV who were initiated on first-line ART and screened for hepatitis B in Mpilo Clinic, Bulawayo, Zimbabwe, 2017–2019

Characteristics	Initiated first-line ART		Screened for HBV		P value
	n	n	n	(%)	
Total	422	361		(85.5)	
Age group, years					
5–14	35	33		(94.3)	0.01
15–24	69	62		(89.9)	
25–49	269	228		(84.8)	
≥50	49	38		(77.6)	
Sex					
Male	181	152		(84.0)	0.43
Female	241	209		(86.7)	
Marital status					
Single	129	116		(89.9)	0.21
Married	211	182		(86.3)	
Divorced/separated	49	41		(83.7)	
Widowed	20	17		(85.0)	
Missing data*	13	5		(38.5)	
Employment status					
Unemployed	194	165		(85.1)	0.15
Employed	155	135		(87.1)	
Student	59	55		(93.2)	
Missing data*	14	6		(42.9)	
Body mass index, kg/m ²					
<18.5	93	84		(90.3)	0.32
18.5–24.99	218	183		(83.9)	
25–29.99	72	61		(84.7)	
≥30	39	33		(84.6)	
CD4 cell count/mm ³					
<200	110	96		(87.3)	0.58
≥200	261	233		(89.3)	
Missing data*	51	32		(62.7)	
Creatinine clearance, ml/min					
<60	40	33		(82.5)	0.15
≥60	356	320		(89.9)	
Missing data*	26	8		(30.8)	
Anaemia					
Yes	165	144		(87.3)	0.41
No	219	197		(90.0)	
Missing data*	38	20		(52.6)	
Alanine transaminase level, U/L					
≤32	278	249		(89.6)	0.11
>32	99	94		(94.9)	
Missing data*	45	18		(40.0)	

*Not included in analysis.

PLHIV = people living with HIV; ART = antiretroviral therapy; HBV = hepatitis B virus.

TABLE 3 Characteristics associated with HBV in PLHIV who were initiated on first-line antiretroviral therapy in Mpilo Clinic, Bulawayo, Zimbabwe, 2017–2019

Characteristics	Screened for HBV		Diagnosed HBsAg-positive		PR (95%CI)	aPR (95%CI)	P value
	n	n	(%)				
Total	361	38	(10.5)				
Age group, years	361	38					
5–14	33	2	(6.1)	0.5 (0.1–2.0)	0.7 (0.1–5.5)	0.73	
15–24	62	5	(8.1)	0.7 (0.3–1.6)	0.6 (0.2–1.8)	0.33	
25–49	228	28	(12.3)	Reference			
≥50	38	3	(7.9)	0.6 (0.2–2.0)	0.7 (0.2–2.3)	0.51	
Sex	361	38					
Male	152	19	(12.5)	Reference			
Female	209	19	(9.1)	0.7 (0.4–1.3)	0.8 (0.4–1.5)	0.44	
Marital status	356	38					
Single	116	14	(12.1)	1.3 (0.7–2.5)	1.5 (0.6–3.5)	0.40	
Married	182	17	(9.3)	Reference			
Divorced/separated	41	7	(17.1)	1.8 (0.8–4.1)	1.5 (0.6–3.7)	0.42	
Widowed	17	0	(0.0)	–			
Employment	355*	38					
Unemployed	165	21	(12.7)	Reference			
Employed	135	12	(8.9)	0.7 (0.4–1.4)	0.78 (0.4–1.7)	0.54	
Student	55	5	(9.1)	0.7 (0.3–1.8)	1.35 (0.3–5.6)	0.42	
Body mass index, kg/m ²	361	38					
<18.5	84	10	(11.9)	1.1 (0.5–2.2)	1.1 (0.5–2.6)	0.86	
18.5–24.99	183	20	(10.1)	Reference			
25–29.99	61	7	(11.5)	1.1 (0.5–2.4)	1.4 (0.6–3.5)	0.50	
≥30	33	1	(3.0)	0.3 (0.1–2.0)	0.5 (0.1–4.0)	0.51	
CD4 cell count/mm ³	329*	38					
<200	96	17	(17.7)	2.0 (1.1–3.6)	1.38 (0.7–2.7)	0.35	
≥200	233	21	(9.0)	Reference			
Creatinine clearance, ml/min	353*	37					
<60	33	5	(15.2)	1.5 (0.6–3.6)	0.91 (0.3–2.6)	0.86	
≥60	320	32	(10.0)	Reference			
Anaemia	341*	37					
Yes	144	25	(17.4)	2.8 (1.4–5.4)	2.3 (1.1–4.7)	0.03	
No	197	12	(6.1)	Reference			
Alanine transaminase level, U/L	343*	38					
>32	94	23	(24.5)	4.1 (2.2–7.4)	2.9 (1.5–5.8)	0.002	
≤32	249	15	(6.0)	Reference			

*Missing data not included in analysis. All variables included in the adjusted model.

HBV = hepatitis B virus; PLHIV = people living with HIV; HBsAg = hepatitis B surface antigen; PR = prevalence ratio; CI = confidence interval; aPR = adjusted PR.

TABLE 4 Treatment regimens of PLHIV who were initiated on first-line ART in Mpilo Clinic, Bulawayo, Zimbabwe, in relation to being screened for and diagnosed with HBV, 2017–2019

Nucleoside/nucleotide reverse transcriptase inhibitor backbone of first-line ART	Total PLHIV		Screened for HBV		Diagnosed HBsAg-positive	
	n	n	(%)*	n	(%)*	
All ART regimens	422	361		38		
Initiated on TDF+3TC backbone	378	324	(89.8)	30	(78.9)	
Initiated on 3TC backbone only	44	37	(10.2)	8	(21.1)	
Initiated on neither TDF or 3TC backbone	0	0	(0)	0	(0)	

*Column percentages.

PLHIV = people living with HIV; ART = antiretroviral therapy; HBV = hepatitis B virus; HBsAg = hepatitis B surface antigen; TDF = tenofovir; 3TC = lamivudine.

TABLE 5 ART regimens that did not include TDF+3TC which were given to eight PLHIV who were HBsAg-positive

ART regimen	PLHIV <i>n</i>	Age years	Reason for ART regimen
ABC+3TC+EFV	6	14, 23, 30, 43, 50, 61	Four had renal impairment and TDF contraindicated Two had unknown reasons
ABC+3TC+LPV/r	1	36	Unknown reason
ZDV+3TC+EFV	1	12	Low body weight below TDF weight threshold of 30 kg

ART = antiretroviral therapy; TDF = tenofovir; 3TC = lamivudine; PLHIV = people living with HIV; HBsAg = hepatitis B surface antigen; ABC = abacavir; EFV = efavirenz; LPV/r = lopinavir/ ritonavir; ZDV = zidovudine.

Being anaemic (aPR 2.3, 95%CI 1.1–4.7) and having a raised serum ALT (aPR 2.9, 95%CI 1.5–5.8) at baseline were significantly associated with being HBsAg-positive.

The NRTI backbones used in first-line treatment in relation to HBV screening and being diagnosed HBsAg-positive are shown in Table 4. A TDF + 3TC-based regimen was used in 378 (90%) PLHIV initiating first-line ART. Of the 44 PLHIV not initiated on a TDF + 3TC-based regimen, 37 (84.1%) were screened for HBV and 8 were diagnosed HBsAg-positive. ART regimens that did not include TDF + 3TC were given to eight PLHIV who were HBsAg-positive (Table 5). Altogether, 7 PLHIV were given ABC + 3TC backbones: in 4 this was because of renal impairment (based on the estimated glomerular filtration rate) and TDF was therefore contraindicated, and in the other 3 PLHIV the reasons were unknown. One PLHIV was given ZDV + 3TC, the stated reason being an inappropriate weight for TDF. The four patients in whom TDF was not contraindicated were traced and placed on a TDF-based regimen.

DISCUSSION

This is the first study in the past 5 years in Zimbabwe to document the prevalence of HBV co-infection among PLHIV who initiated ART for the first time, as well as the ART regimens that were being used. There were some interesting findings.

Under routine programmatic conditions, there were high rates of HBV screening. The only baseline characteristic that showed any association with screening was age, with a high proportion of children screened and rates tailing off in those aged ≥ 50 years. The proportion of those screened who were HBsAg-positive was about 10%, with the highest proportions found in those with anaemia and with elevated serum transaminases levels. It was reassuring to observe that four fifths of those with HIV-HBV co-infection were receiving appropriate treatment with a TDF + 3TC NRTI backbone, while the remainder received partial HBV treatment with a 3TC backbone alone.

The high HBV screening rate may be attributed to the integration of HBV screening with HIV care. Screening was also enhanced by the availability of an onsite laboratory and funding through partnership with a non-governmental organisation. The observed HIV-HBV prevalence was comparable with results from Zimbabwe in 2014,¹⁵ and from other African countries such as Mozambique and Lesotho,^{8,21} but was higher than the prevalence reported from Ghana, Ethiopia and South Africa.^{10,11,22} An earlier study in Zimbabwe with samples collected in 2003–2009 showed a higher HIV-HBV prevalence of 17%.¹⁴ The explanation might be that this was an older population that did not benefit from the national hepatitis B vaccination programme which started in 1999.²³

In our study, sociodemographic factors were not associated with HBV infection; this is in line with findings in Ghana and Tanzania.^{10,24} Several studies have reported an association be-

tween raised serum ALT at baseline and HBV-HIV co-infection.^{21,25–27} This is in line with our findings, and is not surprising as HIV infection promotes both HBV replication and reactivation, leading to a more aggressive natural history of HBV and chronic hepatitis B, which is associated with elevated transaminase levels.¹² While some studies have observed an association between HBV co-infection, male sex and low CD4 cell counts (< 200 cells/mm³),^{9,11,15,28} we did not find any such an association. Instead, anaemia was associated with HBV co-infection in patients initiating first-line ART. Anaemia is associated with advanced HIV disease and severe immunosuppression,^{29,30} and it is this factor that most probably explains the associated link with HBV.

We could not identify any previous studies from Africa specifically on the drugs used to treat HIV-HBV co-infection. It was reassuring to observe that most PLHIV received the appropriate TDF + 3TC NRTI backbone, in line with guidelines. Renal impairment was responsible for approximately half of PLHIV just receiving the 3TC backbone (TDF being contraindicated in these circumstances). Why the remainder was not given TDF is unclear, and more information is needed in future about these treatment selections.

There were several strengths to the study. It was conducted within the routine programme setting and results therefore mimic current practice. Selection bias was minimised by enrolling consecutive PLHIV within the study period. However, there were some limitations. Our results may not be generalisable to the rest of the country owing to the uniqueness of the study setting. Indeed, significant gaps with regards to national hepatitis B diagnosis and treatment were noted during the 2017 rapid assessment on viral hepatitis.³¹ We were not able to conduct the whole spectrum of HBV serological tests to further characterise the infection; as these were not available, we were unable to assess the degree of liver disease associated with being HBsAg-positive, we collected no information about hepatitis B vaccination and HIV viral load was not measured at each follow-up visit. We excluded children aged < 5 years because of difficulties in calculating parameters such as BMI and CD4 cell counts and because data in this group were often incomplete.

Despite these limitations, our study has three practical programmatic implications. First, there is need for formal linkage to care of PLHIV diagnosed with HBV infection to ensure they are all initiated on a TDF + 3TC NRTI backbone whenever possible. Second, since management of HBV co-infection with 3TC monotherapy may lead to viral resistance and fatal flare-ups of viral hepatitis, there is need for the National AIDS Programme to avail alternative regimens when TDF is contraindicated. Already there are alternative drugs that can be used for both HIV and HBV.³² For example, tenofovir alafenamide (TAF) has a much better safety profile with respect to renal adverse events and is effective in patients with 3TC-resistant HBV.^{2,32,33} TAF is now available in Zimbabwe. Finally, if resources are scarce, targeted HBV screening for PLHIV with anaemia and elevated ALT could be considered. HIV-HBV coinfection in Zimbabwe needs more attention. Two recent

African studies have shown a high mortality in PLHIV with HBV coinfection despite ART.^{34,35} Further research is needed to assess what interventions are needed to prevent these deaths.

In conclusion, routine HBV screening performed well, and 10% were diagnosed HbsAg-positive in PLHIV who initiated first-line ART at Mpilo OI Clinic, Bulawayo, Zimbabwe. The majority of PLHIV with HBV co-infection received appropriate treatment with a TDF + 3TC NRTI backbone, with the remainder being treated with a 3TC-only backbone. Practical recommendations are made to improve the screening, diagnosis and management of PLHIV with HBV co-infection.

References

- Schweitzer A, Horn J, Mikolajczyk R T, Krause G, Ott J J. Estimations of worldwide prevalence of chronic hepatitis B virus infection: a systematic review of data published between 1965 and 2013. *Lancet* 2015; 386: 1546–1555.
- Seto W-K, Lo Y-R, Pawlotsky J-M, Yuen M-F. Chronic hepatitis B virus infection. *Lancet* 2018; 392: 2313–2324.
- Lavanchy D. Hepatitis B virus epidemiology, disease burden, treatment, and current and emerging prevention and control measures. *J Viral Hepat* 2004; 11: 97–107.
- Rajbhandari R, Jun T, Khalili H, Chung R T, Ananthkrishnan A N. HBV/HIV co-infection associated with poorer outcomes in hospitalised patients with HBV or HIV. *J Viral Hepat* 2016; 23: 820–828.
- Singh K P, Crane M, Audsley J, Avihingsanon A, Sasadeusz J, Lewin S R. Hepatitis B Virus Co-Infection: epidemiology, pathogenesis and treatment. *AIDS* 2017; 31: 2035–2052.
- Maponga T G, Andersson M I, van Rensburg C J, et al. HBV and HIV viral load but not microbial translocation or immune activation are associated with liver fibrosis among patients in South Africa. *BMC Infect Dis* 2018; 18: 214.
- Platt L, French C E, McGowan C R, et al. Prevalence and burden of HBV co-infection among people living with HIV: a global systematic review and meta-analysis. *J Viral Hepat* 2019 October 11; doi 10.1111/jvh.13217.
- Chambal L M, Gudo E S, Carimo A, et al. HBV infection in untreated HIV-infected adults in Maputo, Mozambique. *PLoS ONE* 2017; 12: e0181836.
- Amidou S A, Dovonou C A, Houehanou C, et al. Impact of HIV status on the overall prevalence of chronic hepatitis B infection in Parakou, Benin. *Pan Afr Med J* 2018; 30: 180.
- Pappoe F, Hagan C K O, Obiri-Yeboah D, Nsiah P. Sero-prevalence of hepatitis B and C viral infections in Ghanaian HIV positive cohort: a consideration for their health care. *BMC Infect Dis* 2019; 19: 380.
- Goa A, Dana T, Bitew S, Arba A. Seroprevalence and associated factors of hepatitis B virus infection among HIV-positive adults attending an antiretroviral treatment clinic at Wolaita Sodo University Referral Hospital. *Hepat Med* 2019; 11: 137–147.
- Yang R, Gui X, Xiong Y, Gao S, Yan Y. Impact of hepatitis B virus infection on HIV response to antiretroviral therapy in a Chinese antiretroviral therapy centre. *Int J Infect Dis* 2014; 28: 29–24.
- Columbia University. Zimbabwe Population-based HIV Impact Assessment (ZIMPHIA), 2015–2016. New York, NY, USA: Columbia University, 2016. https://phia.icap.columbia.edu/wp-content/uploads/2016/11/ZIMBABA-WE-Factsheet_FIN_.pdf.
- Mzingwane M, Mamvura T. Hepatitis B virus seroprevalence and serology patterns in a cohort of HIV positive individuals from Harare, Zimbabwe. *J Viruses* 2014; 2014: 1–5.
- Baudi I, Iijima S, Chin'ombe N, et al. Molecular epidemiology of co-infection with hepatitis B virus and human immunodeficiency virus (HIV) among adult patients in Harare, Zimbabwe. *J Med Virol* 2017; 89: 257–266.
- National Medicines and Therapeutics Policy Advisory Committee (NMT-PAC) and the AIDS and TB Directorate, Ministry of Health and Child Care. Guidelines for antiretroviral therapy for the prevention and treatment of HIV in Zimbabwe. Harare, Zimbabwe: NMT-PAC, 2016.
- World Health Organization. Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection. Recommendations for a public health approach. 2nd ed. Geneva, Switzerland: WHO, 2016.
- Zimbabwe National Statistics Agency. Zimbabwe population census, 2012. Harare, Zimbabwe: ZIMSTAT, 2013.
- World Bank. Gross domestic product (GDP) per capita (current US\$) | Data (2016). Washington DC, USA: World Bank, 2016. <http://data.worldbank.org/indicator/NY.GDP.PCAP.CD?view=chart>
- World Health Organization. Haemoglobin concentrations for the diagnosis of anaemia and assessment of severity. Vitamin and mineral nutrition information system. Geneva, Switzerland: WHO, 2011.
- Mugomeri E, Senauoane M, Ruhanya V, Chin'ombe N, Nyandoro G. Occurrence of HBV/HIV coinfection by laboratory values in Roma, Lesotho. *Germes* 2015; 5: 8–11.
- King J, Hagemester D T. Hepatitis B co-infection in HIV-infected patients receiving antiretroviral therapy at the TC Newman Anti-Retroviral Treatment Clinic in Paarl, Western Cape. *South Afr J HIV Med* 2016; 17: 336.
- Boyle E, King M, Sobek M. ZIPUMS-Demographic and Health Surveys: Version 7. Minneapolis, MN, USA: Minnesota Population Center and ICF International, 2019. <https://doi.org/10.18128/D080.V7>.
- Kamenya T, Damian D J, Hgocho J S, Philemon R N, Mahande M J, Msuya S E. The prevalence of hepatitis B virus among HIV-positive patients at Kilimanjaro Christian Medical Centre Referral Hospital, Northern Tanzania. *Pan Afr Med J* 2017; 28: 275.
- Day S, Odem-Davis K, Mandaliya K, et al. Prevalence, clinical and virologic outcomes of hepatitis B virus co-infection in HIV-1 positive Kenyan women on antiretroviral therapy. *PLoS One* 2013; 8: e59346.
- Iroezindu M O, Agbaji O O, Daniyam C A, Isiguzo G C, Sichei C, Akanbi M O. Liver function test abnormalities in Nigerian patients with human immunodeficiency virus and hepatitis B virus co-infection. *Int J STD AIDS* 2013; 24: 461–467.
- Kye-Doudou G, Nortey P, Malm K, et al. Prevalence of hepatitis B virus co-infection among HIV-seropositive persons attending antiretroviral clinics in the Eastern Region of Ghana. *Pan Afr Med J* 2016; 25 (Suppl 1): 7.
- Bivigou-Mboumba B, Amougou-Atsama M, Zoa-Assoumou S, et al. Hepatitis B infection among HIV infected individuals in Gabon: occult hepatitis B enhances HBV DNA prevalence. *PLoS One* 2018; 13(1): e0190592.
- World Health Organization. WHO case definitions of HIV for surveillance and revised clinical staging and immunological classification of HIV-related disease in adults and children. Geneva, Switzerland: WHO, 2007. https://www.who.int/hiv/pub/guidelines/arv2013/annexes/WHO.CG_annex_1.pdf
- Moyle G. Anaemia in persons with HIV infection: prognostic marker and contributor to morbidity. *AIDS Rev* 2002; 4: 13–20.
- Ministry of Health and Child Care Zimbabwe. Report for the rapid assessment of viral hepatitis in Zimbabwe. Harare, Zimbabwe: Ministry of Health and Child Care, 2017.
- Singh K, Crane M, Audsley J, Lewin S. HIV-hepatitis B virus co-infection: epidemiology, pathogenesis and treatment. *AIDS* 2017; 31(15): 2035–2052.
- Vigano M, Loglio A, Grossi G, Lampertico P. Tenofovir alafenamide (TAF) treatment of HBV, what are the unanswered questions? *Expert Rev Anti Infect Ther* 2018; 16: 153–161.
- Kouame G M, Boyd A, Mohr R, et al. French National Agency for Research on AIDS and Viral Hepatitis (ANRS) 12136 Temprano and ANRS 12240 VarBVA Study Groups. Higher mortality despite early antiretroviral therapy in human immunodeficiency virus and hepatitis B virus (HBV) coinfecting patients with high HBV replication. *Clin Infect Dis* 2018; 66: 112–120.
- Christian B, Fabian E, Macha I, et al. Hepatitis B virus coinfection is associated with high early mortality in HIV-infected Tanzanians on antiretroviral therapy. *AIDS* 2019; 33: 465–473.

Contexte : Il existe peu d'informations relatives au diagnostic et au traitement de l'hépatite B (HBV) chez les personnes vivant avec le VIH (PLHIV) au Zimbabwe en dépit des recommandations selon lesquelles l'association tenofovir (TDF) + lamivudine (3TC) est le plus efficace inhibiteur nucléoside/nucléotide de la transcriptase inverse (NRTI), pierre angulaire du traitement antirétroviral (TAR) des patients atteints des deux infections.

Objectif : Déterminer 1) le nombre de personnes dépistées pour l'antigène HBs (HBsAg); 2) le nombre de personnes diagnostiquées comme positives à l'HBsAg ainsi que leurs caractéristiques de départ ; et 3) les NRTI principales utilisées parmi les PLHIV initiant un TAR de première ligne au service des infections opportunistes de Mpilo Hospital, à Bulawayo, Zimbabwe, entre octobre 2017 et avril 2019.

Schéma : Ceci est étude transversale basée sur des données recueillies en routine.

Marco de Referencia: Existe poca información sobre el diagnóstico y el tratamiento de la infección por el virus de la hepatitis B (HBV) en personas con infección por el VIH (PLHIV) en Zimbabwe, pese a la recomendación de tratar con tenofovir (TDF) + lamivudina (3TC), un tratamiento antirretrovírico (TAR) con una base de análogos nucleosídico y nucleotídico inhibidores de la retrotranscriptasa (NRTI), que es el tratamiento más eficaz en las personas con esta infección doble.

Objetivo: Determinar 1) el número de pacientes con detección sistemática del antígeno de superficie de la hepatitis B (HBsAg); 2) el número de casos con un resultado positivo para el HBsAg y sus características iniciales; y 3) el tipo de tratamiento utilizado a base de NRTI en las PLHIV que iniciaron un TAR de primera línea en el consultorio de infecciones oportunistas del hospital Mpilo de Bulawayo, en Zimbabwe, de octubre del 2017 a abril del 2019.

Método: Fue este un estudio transversal a partir de los datos recogidos sistemáticamente.

Résultats : Il y a eu 422 PLHIV initiant un TAR de première ligne. Leur âge médian a été de 34 ans (IQR 25–43). Parmi eux, 361 (85%) ont eu un dépistage du HBV dont 10% ont été HBsAg-positifs. La positivité du HbsAg a été significativement associée avec une anémie (taux de prévalence ajusté [PRa] 2,3 ; IC95% 1,1–4,7) et avec une élévation des taux d'alanine transaminase (PRa 2,9 ; IC95%, 1,5–5,8). Sur 38 PLHIV diagnostiqués HBsAg-positifs, 30 (79%) ont été mis sous TAR basé sur du TDF + 3TC, 7 ont reçu un TAR basé sur abacavir + 3TC et 1 patient a reçu un TAR basé sur zidovudine + 3TC.

Conclusion : Chez les PLHIV, le dépistage du HBV a bien fonctionné, la prévalence de la coinfection à VIH-HBV a été élevée et la majorité des patients a reçu un traitement approprié pour les deux pathologies. Les recommandations visant à améliorer le dépistage, le diagnostic et le traitement de la coinfection VIH et HBV sont discutées.

Resultados: Se presentaron 422 personas con infección por el VIH que iniciaron TAR de primera línea. La mediana de la edad fue 34 años (IQR 25–43). En 361 de estas personas (85%) se realizó la detección de la HBV y 10% tuvo un resultado positivo para el HBsAg. Este resultado positivo se asoció de manera significativa con anemia (tasa de prevalencia ajustada [aPR] 2,3; IC95% 1,1–4,7) y concentraciones altas de alanina-aminotransferasa (aPR 2,9; IC95% 1,5–5,8). De los 38 pacientes con infección por el VIH y diagnóstico positivo para HBsAg, 30 (79%) iniciaron un TAR a base de TDF + 3TC, en 7 el TAR consistió en abacavir + 3TC y 1 paciente recibió zidovudina + 3TC.

Conclusión: La detección sistemática de la HBV en las personas con infección por el VIH tuvo un buen rendimiento; la prevalencia de coinfección fue alta y la mayoría de los pacientes recibió un tratamiento apropiado para ambas afecciones. Se analizan recomendaciones que pueden mejorar la detección sistemática, el diagnóstico y el tratamiento de la coinfección por el VIH y el HBV.