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Hepatocellular Carcinoma Screening among HIV/HBV-coinfected Individuals: A Pilot Study in Urban Zambia

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BACKGROUND

Chronic hepatitis B virus (HBV) infection is the single most important cause of end-stage liver disease and hepatocellular carcinoma (HCC) in sub-Saharan Africa (SSA).

Six-monthly abdominal ultrasound (AUS) screening allows the early diagnosis of HCC and reduces related mortality. Very few HCC screening programs exist in SSA to date.

We took advantage of an established cohort of HIV/HBV-coinfected individuals in Zambia[1] to pilot an AUS-based screening program in primary care clinics.

METHODS

We enrolled HIV/HBV-coinfected adults on antiretroviral therapy (ART) at two outpatient clinics in Lusaka, Zambia. We performed AUS imaging every 6 months and collected data using a standardized case-report form.

All patients had yearly measurements of liver stiffness using transient elastography (TE; Fibroscan 402®), HBV viral load, HBsAg, HBeAg, and alcohol consumption using the Alcohol Use Disorders Identification Test-Consumption (AUDIT-C).

Table 1. Characteristics at ART start

	n =279
Median age, years (IQR)	34.0 (27.8-39.1)
Female sex (%)	114 (40.9)
Secondary education level or higher (%)	162(58.1)
Overweight body mass index >25.5, n (%)	30 (10.8)
WHO clinical stage 3 or 4 (%)	100 (35.8)
Median CD4+ count, cells/ul (IQR)	245.7 (112-355)
HBeAg seropositive, n (%)	103 (36.9)
Smoking (%)	53 (19.0)
Hazardous alcohol consumption (%)	119 (42.6)
Median ALT, U/L (IQR)	46.7 (18-43)
Median HBV DNA, IU/mL (IQR)	4.88e+07 (288-2610000)
HBV DNA>2,000 IU/mL (%)	114 (40.9)
TE LSM (kPa) >7.0 (%)	61 (21.9)
> 9.4 (%)	23 (8.2)

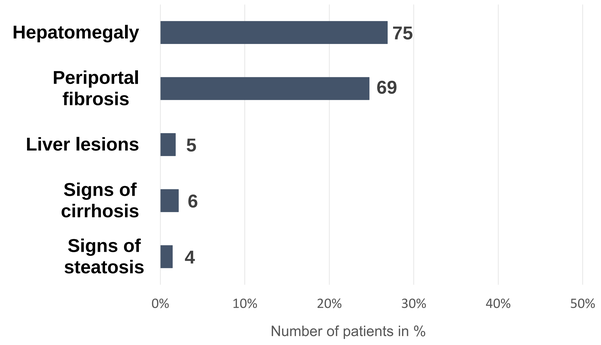
ART = antiretroviral treatment, **IQR** = Interquartile range, **WHO** = World Health Organization, **ALT =** Alanine aminotransferase, **HBV** = Hepatitis B virus, **DNA** = Deoxyribonucleic acid, **TE** = Transient elastography, **LSM** = liver stiffness measurement

- Comprehensive assessment of liver disease including transient elastography and 6-monthly ultrasound-based HCC screening was feasible among 279 HIV/HBV-coinfected individuals in Zambia.
- At the first ultrasound, five patients had liver lesions requiring further imaging investigation.

RESULTS

Of 279 HIV/HBV-coinfected patients included, 114 (40.9%) had HBV DNA levels >2000 IU/mL at initiation of ART. These patients were more likely to have a positive HBeAg (55.0% vs. 18.7%) and significant liver fibrosis (29.8% vs. 23.2%) than those with HBV DNA levels <2000 IU/ml (Table 1).

Figure 1. Main findings at first ultrasound screening



Hepatomegaly was defined as liver diameter >15cm; **patterns of periportal fibrosis** was registered and graded according to the Niamey classification; **signs of cirrhosis** were defined as any of the following: surface nodularity, overall coarse and heterogeneous echotexture, atrophy or segmental hypertrophy; **steatosis** were defined by increased liver echogenicity compared to right kidney parenchyma and beam attenuation.

On first AUS examination, 75 (26.9%) participants had hepatomegaly, 69 (24.7%) periportal fibrosis, 6 individuals (2.2%) showed signs of cirrhosis, and 4 (1.4%) had liver steatosis.

Five (1.8%) patients had a liver lesion >1cm, of whom one participant had significant fibrosis and one had cirrhosis (according to TE). All patients with focal lesions >1cm were referred for further investigation by 4-phase CT scan. Characteristics at ART starts of patients with lesions and features of liver lesions are shown in Table 2.

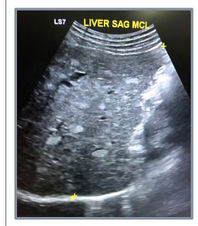
In the majority of patients with elevated liver stiffness no signs of liver cirrhosis were found on ultrasound.

Table 2. Characteristics of patients with liver lesions

Patient	Sex	Age	CD4+ Count (cells/ul)	HBe Ag	HBV DNA (IU/mL)	TE	Type lesion	No. lesions	Largest lesion (cm)
1	M	35	135	pos	52	F0	Hyperechoic	Single	2.2
2	M	29	174	neg	n.d.	F0	Hyperechoic	Single	1.7
3	M	38	237	neg	16600	F0	Hyperechoic	Single	1.4
4	M	47	259	neg	171	F0	Hyperechoic	Single	1
5	M	34	171	pos	39356310	F4	Hypo- and Hyperechoic	Multiple	2.1

HBV = Hepatitis B virus, **DNA** = Deoxyribonucleic acid, **TE** = Transient elastography
Fibrosis stage **F0-F4** was graded according to the **METAVIR scoring** system.

RESULTS



Picture 1. Ultrasound

Picture 1 shows the AUS examination of patient no. 5 (Table 2). A heterogeneous echotexture, surface nodularity of the liver and multiple focal hypo- and hyperechoic focal observations were noted.

On 4-phase CT scan lesions did not present any diagnostic HCC hallmarks.

Conclusion

We report results from one of the first HCC screening programs among HBV-infected individuals in SSA.

About 2% of HIV/HBV-co-infected adults on ART had a significant liver lesion, and a quarter had periportal fibrosis, suggestive of schistosomiasis-induced liver damage.

References

[1] Vinikoor, M.J., et al., *Association between hepatitis B co-infection and elevated liver stiffness among HIV-infected adults in Lusaka, Zambia.* Trop Med Int Health, 2016. **21**(11): p. 1435-1441.

ADDITIONAL KEY INFORMATION

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