

## Original research

# Management of chronic hepatitis B in Uganda: A five-year experience following the initiation of a national sensitization and care campaign

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## ABSTRACT

Despite having the highest Hepatitis B Virus (HBV)-related mortality globally, sub-Saharan Africa (SSA) has been slow in its disease elimination campaign. We describe a 5-year experience in HBV management at a large facility in Uganda and how it can inform future management strategies.

HBV-related patient data were abstracted from clinic records. Of 2664 patients, 1828 (68.6 %) had documented chronic HBV infection. Participants were young, mean age ( $\pm$ SD) 31.3 ( $\pm$ 10.6) and equally split by gender. Overall, 423 (23.1 %) were on antiviral medications including 158/229 (69.0 %) with a sonographic diagnosis of cirrhosis and 130/282 (46.1 %) with Aspartate aminotransferase to Platelet Ratio Index (APRI) score  $\geq 0.5$ . 48/1828 (2.6 %) had Hepatocellular Carcinoma (HCC).

In multivariable analysis, APRI score  $\geq 0.5$  [OR (95 % CI) = 1.76 (1.26–2.46),  $p < 0.01$ ], elevated alanine aminotransferase (ALT) [OR (95 % CI) = 2.25 (1.35–4.47),  $p = 0.04$ ], and HBV viral load  $\geq 2,000$  IU/mL [OR (95 % CI) = 2.97 (1.68–5.22),  $p < 0.01$ ] were predictors of cirrhosis/HCC. Also, an APRI score of  $\geq 0.5$  [OR (95 % CI) = 1.62 (1.19–2.22),  $p = 0.01$ ], elevated ALT [OR (95 % CI) = 2.60 (1.23–5.49),  $p = 0.02$ ], cirrhosis [OR (95 % CI) = 21.65 (9.26–50.59),  $p < 0.01$ ], and viral load  $\geq 2,000$  IU/mL [OR (95 % CI) = 6.62 (3.93–11.15),  $p < 0.01$ ] were associated with antiviral use.

Cirrhosis/HCC apparently occur at lower APRI scores in SSA suggesting need for urgent adoption of the 2024 WHO guidelines which provide for earlier initiation of anti-HBV therapy.

## 1. Background

Recent data indicate that hepatitis B and C were responsible for 125,000 deaths in the sub-Saharan Africa (SSA) region in 2020.<sup>1</sup> In the same year, liver diseases were reported as the 9th leading cause of death in Uganda, claiming over 5000 lives.<sup>2</sup> It is estimated that 72.5 million people in the World Health Organization (WHO) Afro region are infected with chronic viral hepatitis, 64.7 million of whom are specifically infected with hepatitis B (HBV).<sup>3</sup> In Uganda, the HBV disease prevalence is estimated at 4.1 % with the burden varying by region.<sup>4</sup> Due to poor accessibility to viral screening, care, and treatment services, this statistic is likely to be an underestimate.<sup>5,6</sup> Without proper management, approximately 20 % of HBV-infected persons will die early due to liver

disease-related complications such as liver failure, decompensated cirrhosis and Hepatocellular Carcinoma (HCC). Indeed, the Center for Disease Analysis Foundation estimates that in the SSA region, HBV infections claim 12 lives every hour.<sup>7</sup>

Following the recognition of the seriousness of HBV infection in low resource settings by the World Health Assembly<sup>8</sup> and subsequently the need to eliminate it as a public health threat,<sup>9</sup> the World Health Organization (WHO) spearheaded a campaign to eliminate this infection as a public health problem by 2030.<sup>10</sup> As this campaign gained momentum in 2017, Uganda as a member country implemented population sensitization, enhanced screening measures, better access to care for infected persons, re-training programs for health care providers, and improved accessibility to laboratory services and antiviral medications. These

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initiatives complemented earlier efforts of vaccinating infants and screening donor blood for HBV.

Uganda developed a guideline modelled after the 2015 WHO guidelines for the prevention, care, and treatment of persons with chronic HBV infection.<sup>11,12</sup> Briefly, this guideline considered decompensated cirrhosis, HIV co-infection, Aspartate aminotransferase to Platelet Ratio index (APRI) score  $>2.0$ , HBV DNA  $>20,000$  IU/mL with elevated Alanine aminotransferase (ALT) and age  $>30$  years in assessing patients as eligible to commence antiviral medications for HBV infection.<sup>12</sup>

The Government through its Central Public Health Laboratories also offers free quantitative HBV viral load testing, with each patient being eligible for at least one round of testing every year. Government-run hospitals also provide free blood testing for HIV, liver function, and renal function as well as a complete blood count as prerequisites for patients' evaluation for treatment eligibility.

After half a decade of implementation and achieving the above strides in HBV prevention and care, we conducted a retrospective study at a liver clinic in one of the two national centres of excellence for HBV care based at a large national referral hospital in Kampala, Uganda. We reviewed the five-year experience of managing chronic HBV infection to inform future strategies.

## 2. Methods

This study was conducted at Kiruddu National Referral Hospital in Uganda. The facility is mandated to offer specialist services including a dedicated liver disease clinic, which has been in operation since 2016. This clinic runs once weekly and offers services to adults with HBV mono-infection. HBV/HIV dual infected individuals are, by policy, treated in the HIV clinic. It is common practice to refer HIV-infected adults with overt liver diseases for care in the liver clinic.

In this retrospective study, medical records of patients attending the above clinic over a 5-year period (2018–2022) were retrieved and data relevant to HBV management were abstracted. The variables captured from these charts included: social demographic variables (age at registration in the clinic, sex), hepatitis B surface antigen test (HBsAg) result, the most recent Human Immunodeficiency Virus (HIV) status result, Hepatitis C Virus (HCV) antibody and viral load tests, Hepatitis D Virus (HDV) antibodies, liver enzyme levels, platelet counts, hepatitis B e antigen (HBeAg), hepatitis B viral load levels, alpha-feto protein (AFP) levels, abdominal ultrasound scan results, abdominal CT findings, any evidence of decompensated liver disease (ascites, hepatic encephalopathy, upper gastrointestinal tract bleeding) or HCC, and use of antiviral medications (tenofovir (TDF) monotherapy or a combined pill of TDF and lamivudine). The combined pill is used when the hospital runs low on TDF and is also the recommended treatment approach (together with a third anti-retroviral medication) for HIV/HBV co-infected patients. Only individuals diagnosed with HBV via a confirmatory HBsAg and/or hepatitis B viral load test results were included in this study.

Using the above data (liver enzymes and platelet counts), we assessed the eligibility of our study participants for antiviral medications by computing their APRI score using the formula  $APRI = (AST/ULN) \times 100 / \text{Platelet count} (10^9/L)$ . In line with data suggesting that the WHO 2015 guideline recommendation of initiating antiviral medications at an APRI cutoff of  $>2$  deny  $>50$  % of eligible patients treatment,<sup>13</sup> and in view of the recent revisions to this guideline,<sup>14,15</sup> we used the suggested APRI score of  $\geq 0.5$  as surrogate for significant fibrosis. The outcomes of this study were defined as the occurrence of liver complications (cirrhosis and/or HCC) and the use or non-use of antiviral medications for HBV.

**Statistical analysis:** Data were captured in an excel sheet and exported to STATA software package, version 14.0 (College Station, Texas, USA) for analysis. Descriptive characteristics of the participants were summarized. Frequencies and percentages of the categorical variables were established while means (standard deviation) were obtained

for the continuous variables. The diagnosis of liver cirrhosis was based on liver sonography while that of HCC was based on suggestive clinical findings supported by liver sonography, triphasic abdominal CT scan and in some few cases liver histopathology. Eligibility for antiviral medications was based on the APRI score criterion (cut-off  $>0.5$ ) and on sonographic liver findings. Logistic regression analysis was used to assess the association of the variables to the above outcomes. Variables with a p-value  $<0.2$  were included in multivariable logistic regression analysis. Results of the association of the variables to the outcome were summarized as odds ratios, with 95 % confidence intervals (CIs) and p-values. Statistical significance was considered at a 2-sided p-value of  $\leq 0.05$  and 95 % CIs excluding one.

This study was approved by the Mildmay Uganda Research and Ethics Committee (approval REC Ref 0201–2023). Administrative clearance was granted by Kiruddu National Referral Hospital administration.

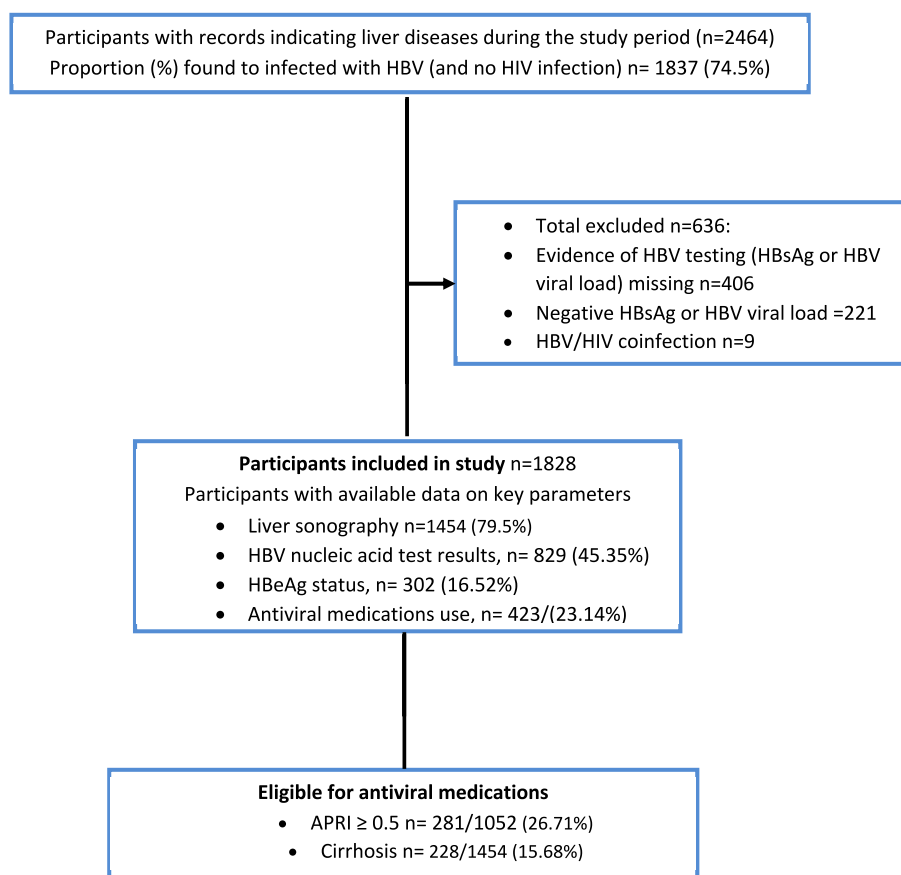
## 3. Results

In the period from July through November 2023, a chart review was conducted at the liver clinic at Kiruddu National Referral Hospital in Uganda for patients with a diagnosis of HBV over the 5-year period from 2018 to 2022. Of the 2464 potential participants whose records were accessed, 1837 (74.5 %) had a positive HBsAg test. Of these, 9 were co-infected with HBV and HIV. No HBV diagnosis was made using only the HBV viral load in the absence of a positive HBsAg test. 636/2464 patient records (25.81 %) were excluded either because they were HBsAg negative ( $n = 221$ ), their HBsAg or HBV viral load tests were missing ( $n = 406$ ), or there was coinfection with HIV ( $n = 09$ ). A total of 1828 patient records were included in the study (Fig. 1).

The study population was generally young; mean age ( $\pm$  SD), 31.3 ( $\pm 10.6$ ) and split almost equally by gender. Over two-thirds 1266/1828 (69.26 %) of the participants had either normal or marginally elevated ALT levels (less than two-times the upper limit of normal). Of the 302/1828 participants for whom HBeAg test results were available, close to three quarters 225/302 (74.5 %) had HBeAg-negative disease. Comorbidity with alcoholic liver disease and schistosomiasis occurred in less than 1 % of participants. With regard to routine screening for other hepatotropic viruses specifically HCV and HDV, 134/1828 (7.33 %) had an anti-HCV screening test; 13 of these were anti-HCV positive, but only 4 had nucleic acid testing -all had active infection. Only 0.22 % (4/1828) had an anti-HDV screening test, 2 of which were anti-HDV positive. Overall, evidence for screening for HCC using alfa feto protein was available for 52 of 1828 (2.84 %) of the reviewed patient charts (Table 1).

Regarding patient evaluation for antiviral medication use eligibility and disease complications, 873/1828 (47.8 %) had at least one HBV viral load test. Over three-quarters 1454/1828 (79.54 %) had liver sonography performed, and 1052/1828 (57.55 %) had both complete blood count (CBC) and liver biochemistry parameters that could facilitate the computation of APRI scores. Of those that had liver sonography, 228/1454 (15.6 %) were deemed to have cirrhosis. On the other hand, 281/1052 (26.7 %) for whom the APRI score was computed had cirrhosis. In total, 423 (23.1 %) were on antiviral medications. Of these 158/423 (38 %) had liver cirrhosis. HCC was diagnosed in 48 of the 1828 patients (2.6 %) (Table 1). Both cirrhosis and HCC tended to occur at a young age; mean ( $\pm$  SD) age; 35.4 ( $\pm 11.11$ ) and 36.23 ( $\pm 10.73$ ) for cirrhosis and HCC respectively.

In bivariable analysis, male gender [OR (95 % CI) = 2.99 (2.24–3.98),  $p < 0.01$ ], age  $>35$  years; 35–49 [OR (95 % CI) = 2.11 (1.55–2.87),  $p < 0.01$ ],  $\geq 50$  [OR (95 % CI) = 4.51 (2.71–7.52),  $p < 0.01$ ], liver fibrosis (APRI score  $\geq 0.5$ ) [OR (95 % CI) = 14.26 (9.13–22.27),  $p < 0.01$ ] alcoholic liver disease [OR (95 % CI) = 18.74 (3.96–88.77),  $p < 0.01$ ], elevated ALT [OR (95 % CI) = 3.30 (2.17–5.01),  $p < 0.01$ ], AST [OR (95 % CI) = 9.76 (6.64–14.35),  $p < 0.01$ ], and elevated HBV viral load  $>2,000$  IU/mL [OR (95 % CI) = 4.81



**Fig. 1.** Flowchart of selected participants

HBeAg = hepatitis B e antigen, APRI = aspartate aminotransferase to platelet ratio index, Antiviral medications = tenofovir monotherapy or tenofovir in combination with lamivudine. Of the 1454 that had liver sonography, 15.68 % (228/1454) had features suggestive of cirrhosis. Relatedly, 26.71 % (281/1052) whose APRI score was evaluated had cirrhosis at a cut-off score of  $\geq 0.5$ .

(3.01–7.72),  $p < 0.01$ ) were associated with cirrhosis/HCC (Table 3).

With regard to antiviral medication use, male gender [OR (95 % CI) = 2.04 (1.63–2.56),  $p < 0.01$ ], age  $>35$  years, 35–49 [OR (95 % CI) = 1.96 (1.55–2.53),  $p < 0.01$ ];  $\geq 50$  [OR (95 % CI) = 3.59 (2.31–5.60),  $p < 0.01$ ] a positive HBeAg status, [OR (95 % CI) = 3.94 (2.25–6.91)  $p < 0.01$ ], APRI score  $>0.5$  [OR (95 % CI) = 9.04 (6.42–12.75),  $p < 0.01$ ], cirrhosis [OR (95 % CI) = 12.32 (8.93–17.00),  $p < 0.01$ ], alcoholic liver disease [OR (95 % CI) = 5.04 (1.41–17.94),  $p < 0.01$ ], elevated transaminases; ALT [OR (95 % CI) = 4.17 (3.31–6.70),  $p < 0.001$ ], AST [OR (95 % CI) = 5.15 (3.70–7.19),  $p < 0.01$ ], and a high HBV viral load  $>2,000\text{IU/mL}$  [OR (95 % CI) = 8.74 (6.09–12.55),  $p < 0.01$ ] were associated with antiviral use (Table 3).

In multivariable analysis, only an APRI score of  $\geq 0.5$  [OR (95 % CI) = 1.65 (1.17–2.32),  $p < 0.01$ ], elevated ALT [OR (95 % CI) = 2.08 (1.53–2.84),  $p = 0.04$ ], and a high viral load [OR (95 % CI) = 2.08 (1.53–2.84),  $p < 0.01$ ] emerged as predictors of cirrhosis/HCC. On the other hand, APRI scores of  $\geq 0.5$  [OR (95 % CI) = 1.48 (1.08–2.04),  $p = 0.01$ ], elevated ALT [OR (95 % CI) = 2.46 (1.13–5.34),  $p = 0.02$ ], cirrhosis [OR (95 % CI) = 20.44 (8.62–48.46),  $p < 0.01$ ] and high viral loads [OR (95 % CI) = 3.36 (2.50–4.50),  $p < 0.01$ ] were predictors of antiviral medication use (Table 4).

#### 4. Discussion

In this study we have demonstrated that a high proportion of patients with chronic liver disease in the clinic were infected with HBV which was further complicated by liver fibrosis/cirrhosis and HCC. Ongoing sensitization about the HBV disease has led to increased HBV screening at both health facility and community levels, however it clearly remains

a threat to the public. The high cirrhosis/HCC burden found to occur at such a low mean age threatens the lives of young adults in their most productive years of life and re-kindles a need for a concerted effort to improve access to diagnostic, preventive and treatment facilities for HBV and its associated complications.

Assessing patients for treatment eligibility remains a challenge in SSA and other low resource settings. In such settings, the use of non-invasive methods of diagnosing liver fibrosis in determining eligibility to antiviral medications has been recommended as an alternative to the rather invasive and expensive liver biopsy that is commonly used in the high resource countries.<sup>11</sup> Traditionally, an APRI score of  $>2$  has been used as a surrogate for liver fibrosis. However, more recent data including that from Africa<sup>13,16,17</sup> and Asia highlighted diagnostic challenges at this cut-off threshold and improved diagnostic accuracy at a much lower APRI threshold.<sup>18</sup> The WHO revised this threshold downwards to  $>0.5$  in its recent guideline.<sup>14,15</sup> In line with our objective to analyze and use these data to inform future HBV treatment strategies in low-income settings, this study, opted to use the lower APRI score cut-off value of  $\geq 0.5$  to define fibrosis and a lower HBV viral load of 2,000IU/mL as a threshold for initiating antiviral medications. We have indeed demonstrated an association of the APRI score at this threshold with liver cirrhosis/HCC, and the newly revised HBV viral load threshold (from 20,000 to 2,000IU/mL) for considering treatment initiation as predictors of liver fibrosis, supporting recent revision of the WHO guideline.<sup>14,15</sup> By bridging the previously identified gaps in which many eligible HBV-infected individuals in African countries were not receiving antiviral medications,<sup>13,19–22</sup> this move would afford a larger proportion of HBV-infected persons in low resource settings access to timely antiviral medications, consequently lowering their risk of

**Table 1**  
DESCRIPTIVE characteristics of the study population (N = 1828).

Variable	N (%)
Sex <sup>a</sup>	
Females	912 (49.98)
Males	916 (50.11)
Age years (mean (+/- SD)	31.3 (+/- 10.6)
Hepatocellular carcinoma	48 (2.63)
Alfa feto protein	52 (2.84)
Hepatitis D antibody <sup>a</sup>	4 (0.22)
Schistosomiasis	12 (0.66)
Hepatitis C (viral load).	4 (0.22)
Alcoholic liver disease	10 (0.55)
Liver sonography	1454 (79.5)
Sonography <sup>b</sup>	
Evidence of cirrhosis	228 (12.47)
Normal	1208 (66.08)
APRI score <sup>c</sup>	
≥0.5	281 (16.55)
<0.5	771 (42.18)
Antiviral therapy (tenofovir) use	
Yes	423 (23.14)
No	1405 (76.86)
ALT (IU/mL) <sup>d</sup>	
≥2XULN	150 (8.21)
<2XULN	1266 (69.26)
AST (IU/mL) <sup>e</sup>	
≥2XULN	175 (9.57)
<2XULN	1243 (68.00)
Hepatitis B e antigen <sup>f</sup> Pos	77 (4.21)
Neg	225 (12.31)
Hepatitis B viral load	
Missing	999
Detectable	829 (47.7)
HBV Viral load (IU/mL) <sup>g</sup>	4112.21 (3009.62–5618.74)

Missing data: <sup>a</sup> hepatitis D antibody 1824 (99.78 %), <sup>b</sup> Liver sonography 392 (21.44 %), <sup>c</sup> APRI score 776 (42.45 %), <sup>d</sup> ALT 412 (22.54 %), <sup>e</sup> AST 410 (22.43 %), <sup>f</sup> HBeAg 1526 (83.48). <sup>g</sup> Geometric mean and 95 % confidence intervals of 828 hepatitis B-infected individuals whose viral load was above the lower limit of detection of the assay.

**Table 2**  
Proportion of eligible participants that were receiving antiviral medications.

Variable and measure of eligibility among HBV -infected participants	Number eligible for antiviral medications N	Eligible and receiving antiviral medications n (%)	Number not eligible for antiviral medications N	Not Eligible but receiving medications n (%)
APRI score ≥0.5	281	130/282 (46.10)	771	68/771 (8.82 %)
Ultrasound scan Cirrhosis	228	158/228 (69.30)	1208	188/1208 (15.56)

progression to cirrhosis and its attendant complications. It is promising to note that liver enzyme elevation and the above predictors of liver disease complications in this study were also found to be associated with the use of antiviral medications (Table 2). High viral load >2,000IU/mL and elevated ALT levels have been found to be independent predictors of liver fibrosis in previous studies in Ethiopia and elsewhere.<sup>23,24</sup> Although factors such as age and male gender were previously found to predict liver fibrosis in the Ethiopian study, we only found an association on univariate analysis and not at multivariate analysis. Unlike our study which considered a cut-off P value < 0.2 at bivariate analysis for inclusion in multivariable analysis, the Ethiopian study considered a lower P-value cut-off of 0.1. Initiating antiviral medications for persons with the above predictors is consistent with

**Table 3**  
Bivariable logistic regression analysis of factors associated with CIRRHOSIS/HCC and use of antiviral medications among hepatitis B infected patients.

	Bivariable model for HBV-related complications (cirrhosis/hepatocellular carcinoma) N = 262		Bivariable model for HBV-antiviral medication use N = 423	
	Odds Ratio (95 % CI)	P-value	Odds Ratio (95 % CI)	p-value
Gender				
Women	Ref		Ref	
Men	2.99 (2.24–3.98)	<0.01	2.04 (1.63–2.56)	<0.01
Age				
<35	Ref		Ref	
35–49	2.11 (1.55–2.87)	<0.01	1.96 (1.55–2.53)	<0.01
≥50	4.51 (2.71–7.52)	<0.01	3.59 (2.31–5.60)	<0.01
Hepatitis B e antigen				
negative	Ref		Ref	
positive	1.64 (0.72–3.71)	0.24	3.94 (2.25–6.91)	<0.01
APRI score				
<0.5	Ref		Ref	
≥0.5	14.26 (9.13–22.27)	<0.01	9.04 (6.42–12.75)	<0.01
Ultrasound scan				
No cirrhosis	N/A		Ref	
cirrhosis			12.32 (8.93–17.00)	<0.01
Schistosoma				
Negative	Ref		Ref	
Positive	0.91 (0.20–4.17)	0.90	0.66 (0.14–3.04)	0.60
Alcoholic liver disease				
Negative	Ref		Ref	
Positive	18.74 (3.96–88.77)	<0.01	5.04 (1.41–17.94)	0.01
ALT				
<2XULN	Ref		Ref	
≥2XULN	3.30 (2.17–5.01)	<0.01	4.17 (3.31–6.70)	<0.01
AST				
<2XULN	Ref		Ref	
≥2XULN	9.76 (6.64–14.35)	<0.01	5.15 (3.70–7.19)	<0.01
HBV viral load				
<2000	Ref		Ref	
≥2000	3.17 (2.03–4.96)	<0.01	5.1 (3.68–7.06)	<0.01

**Table 4**  
Multivariable logistic regression analysis of factors associated with CIRRHOSIS/HCC and use of antiviral medications among hepatitis B infected patients.

	Multivariable model for complications (cirrhosis/HCC)		Multivariable model for Antiviral use	
Parameter	OR <sub>adj</sub>	P-value	OR <sub>adj</sub>	p-value
Gender	1.39 (0.79–2.45)	0.32	1.61 (0.97–2.70)	0.06
Age	1.10 (0.68–1.79)	0.67	1.23 (0.79–1.91)	0.35
APRI score ≥ 0.5	1.76 (1.26–2.46)	<0.01	1.62 (1.19–2.22)	<0.01
ALT	2.25 (1.35–4.47)	0.04	2.60 (1.23–5.49)	0.01
Hepatitis B e antigen	–	–	0.99 (0.72–1.37)	0.97
Cirrhosis	–	–	21.65 (9.26–50.59)	<0.01
HBV viral load	2.97 (1.68–5.22)	<0.01	6.62 (3.93–11.15)	<0.01

major Asian American and European liver association guidelines, in which these parameters are part of the key considerations for initiating antiviral treatment.<sup>25–27</sup>

In this study, 423/1828 (23 %) of the participants were on antiviral



medications. This proportion is similar to findings in other settings.<sup>20</sup> Of note, close to 40 % (158/432) of those on treatment had liver cirrhosis. This finding is similar to data from another hospital-based study in an Ethiopian cohort where cirrhosis was the most common indication for initiating treatment over a 5-year period.<sup>28</sup> Unlike our study which considered abdominal sonography to diagnose cirrhosis, the Ethiopian study employed the more sensitive and specific liver elastography to diagnose liver cirrhosis and fibrosis. This late presentation for care in SSA represents a missed opportunity for patients to benefit from the potential reversal of liver fibrosis and the prevention of cirrhosis and HCC that are associated with timely initiation of medications.<sup>29</sup>

Despite the above strides, we still found delayed initiation of antiviral medications for some eligible persons. This mirrors the findings from an earlier study in Northwestern Uganda.<sup>19</sup> Similar gaps in patient evaluation and accessing antiviral medications have been documented elsewhere in SSA<sup>30,31</sup> and highlight the need for better health care systems, ongoing education of clinicians on HBV management, and an uninterrupted supply of medications.

In developed countries, it is standard practice to screen individuals with chronic HBV for HCV, HDV, and HCC. Though advocated for in several guidelines,<sup>11,12,26,27</sup> it is not routinely done in many settings in SSA due to resource constraints. Indeed, glaring gaps in screening for all the above conditions were eminent in this study. In the absence of data on the national HCV prevalence and a recent blood bank study showing a high HCV disease burden,<sup>32</sup> it may be worth screening individuals with chronic HBV in Uganda for this potentially curable infection<sup>33</sup> which has dire consequences to liver health, especially in the setting of HBV co-infection.<sup>34</sup> The identification of HCV infected persons and their treatment will add momentum to the ongoing campaign to eliminate viral hepatitis by 2030. However, treatment for HCV infection is not yet freely available to patients in Uganda and other low resource settings in Africa.

Alcoholic liver disease was an important predictor of both cirrhosis and antiviral use in this sub-population. This is not surprising in a country which is believed to be one of the top most consumers of alcohol in the world.<sup>35</sup> In addition, alcohol misuse has also been found to be associated with poor adherence to medications for chronic diseases such as HBV.<sup>36</sup> A root cause analysis of the drivers of alcohol abuse could be an important step in informing preventive measures.

Though schistosomiasis and HBV are endemic to Uganda, very few participants in this study were coinfecting with both diseases. This could be attributed to the fact that schistosoma-infected patients that present to our clinic are a small and highly selected sub-population that has complications of portal hypertension (ascites or bleeding esophageal varices) or differences in the modes of transmission of these diseases. The effect of the interaction of schistosoma and HBV on liver disease progression in our setting has not been well studied. Elsewhere, previous observational studies on this interaction have yielded contradicting results, with some suggesting a more aggressive disease course and others no impact on liver pathology.<sup>37,38</sup>

Our study has some limitations. We used data from a single centre that was not originally acquired to answer our research question; consequently, there was missing and incomplete data on some study parameters leading to both selection and information bias. In addition, we did not control for all the possible confounder variables in the analysis with a possibility of residual confounding. Although a randomized control study design could ensure even distribution of confounder variables in the study arms and avoid both selection and information bias, the study design would be unethical as some interventions which have already been deemed beneficial would be denied to respondents in the comparison arm. We were also unable to assess variables such as serial liver enzyme levels to ascertain persistently elevated ALT levels which in combination with HBV viral load levels would constitute another criteria for antiviral medication use. This reflects the challenges of medical care provision in the resource limited setting where financial constraints frequently deter clinicians from conducting all the required assessment tests for the patients. The

temporal association of the measured variables to the occurrence of cirrhosis/HCC or initiation of antiviral medications could not be ascertained. However, we did access a large volume of data from a centre of excellence for HBV management in Uganda, a WHO model country for HBV care in SSA. Our study findings therefore offer a good insight into the factors associated with HBV-related liver complications and antiviral use in resource poor settings of SSA.

In conclusion, a high proportion of patients with HBV in this study have cirrhosis as determined by sonography or a much-lower APRI threshold of  $\geq 0.5$ . In addition, many patients in chronic care are not fully evaluated for eligibility for treatment. Even among those that are eligible for antiviral medications including those with cirrhosis, a sizeable proportion were not initiated on treatment.

These findings demonstrate the need to accelerate the implementation of preventive measures for HBV, thorough evaluation of HBV-infected individuals for eligibility for antiviral medications. Adoption of the recent 2024 WHO HBV management guideline that allows for the initiation of antiviral medications at a lower APRI score threshold could potentially be a pivotal step in achieving the WHO-driven goal to eliminate HBV as a public health threat in low resource settings by 2030.

### CRedit authorship contribution statement

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### Declaration of competing interest

**Declaration:** The authors declare no conflict of interest.

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### Data availability

Data will be made available on request.

### References

1. World Health Organization. "91 million Africans infected with Hepatitis B or C." <https://www.afro.who.int/news/91-million-africans-infected-hepatitis-b-or-c>; 2022. Accessed February 3, 2025.

2. World Health Organization. World health rankings. Uganda: liver disease. Available at: <https://www.worldlifeexpectancy.com/uganda-liver-disease>; 2020. Accessed February 4, 2025.
3. Global hepatitis report 2024. *Action for Access in Low- and Middle-Income Countries*. Geneva: World Health Organization; 2024.
4. Ministry of Health, Uganda. *Uganda Population-Based HIV Impact Assessment (UPHIA) 2016-2017: Final Report*. Kampala: Ministry of Health; July, 2019.
5. Faniyi AA, Okesanya OJ, Manirambona E, et al. Advancing public health policies to combat Hepatitis B in Africa: challenges, advances, and recommendations for meeting 2030 targets. *J Med, Surg Public Health*. 2024;2, 100058.
6. Sonderup MW, Spearman CW. *HBV Elimination in Africa-Current Status and Challenges*. vol. 23. 2024, e0166.
7. CDA foundation's polaris observatory. Last updated: December 21st, 2020. Available at: [https://cdafound.org/dashboard/polaris/dashboard\\_regions.html](https://cdafound.org/dashboard/polaris/dashboard_regions.html); 2019. Accessed February 4, 2025.
8. World Health Organization. Resolution WHA63.18. Viral hepatitis. In: *Sixty-third World Health Assembly, Agenda Item 11.12, 21 May 2010*. Geneva: WHO; 2010. [http://apps.who.int/gb/ebwha/pdf\\_files/WHA63-REC1/WHA63\\_REC1-en.pdf](http://apps.who.int/gb/ebwha/pdf_files/WHA63-REC1/WHA63_REC1-en.pdf). Accessed February 3, 2025.
9. World Health Organization. Resolution WHA67.6. Viral hepatitis. In: *Sixty-seventh World Health Assembly, Agenda Item 12.3 May 2014*. Geneva: WHO; 2014. [https://apps.who.int/gb/ebwha/pdf\\_files/WHA67-REC1/A67\\_2014\\_REC1-en.pdf](https://apps.who.int/gb/ebwha/pdf_files/WHA67-REC1/A67_2014_REC1-en.pdf). Accessed February 3, 2025.
10. *Global Health Sector Strategies on, Respectively, HIV, Viral Hepatitis and Sexually Transmitted Infections for the Period 2022-2030*. Geneva: World Health Organization; 2022.
11. Uganda Guidelines for Prevention. *Testing, Care and Treatment of Hepatitis B and C Virus Infection*. 2019.
12. World Health Organization WHO. *Guidelines for the Prevention, Care and Treatment of Persons with Chronic Hepatitis B Infection*. Geneva: World Health Organization; 2015.
13. Abera H, Desalegn H, Berhe N, et al. The WHO guidelines for chronic hepatitis B fail to detect half of the patients in need of treatment in Ethiopia. *J Hepatol*. 2019;70: 1065–1071.
14. *Guidelines for the Prevention, Diagnosis, Care and Treatment for People with Chronic Hepatitis B Infection*. Geneva: World Health Organization; 2024. Licence: CC BY-NC-SA 3.0 IGO.
15. Easterbrook PJ, Luhmann N, Bajis S, et al. WHO 2024 hepatitis B guidelines: an opportunity to transform care. *The Lancet Gastroenterology Hepatology*. 2024;9: 493–495.
16. Eloumou SAFB, Nga TWB, Ndam AN, et al. Evaluation of NonInvasive markers of liver fibrosis in chronic hepatitis B patients in a SubSaharan african setting: transient elastography versus APRI, FIB4, GTT/platelet scores. *Open J Gastroenterol*. 2023;13: 209–224. <https://doi.org/10.4236/ojgas.2023.136020>.
17. Kabamba-Tshikongo A, Baleebenga A, Kalunga-Tomba B, et al. Comparative evaluation of APRI and MELD scores in the prediction of complications of chronic hepatitis in patients infected with hepatitis B or C viruses in Lubumbashi, democratic republic of Congo. *J Clin Virol*. 2025;5, 100200.
18. Luo H, Peng S, Ouyang W, et al. Assessment of liver fibrosis by transient elastography and multi-parameters model in young children with chronic hepatitis B virus infection. *BMC Infect Dis*. 2022;22:160.
19. Seremba E, Wandera C, Ssekitoleko R, et al. Antiviral use among hepatitis B infected patients in a low resource setting in Africa: a case study of West Nile. *Uganda African Health Sci*. 2023;23:169–178.
20. Tan M, Bhadoria AS, Cui F, et al. Estimating the proportion of people with chronic hepatitis B virus infection eligible for hepatitis B antiviral treatment worldwide: a systematic review and meta-analysis. *The lancet Gastroenterology Hepatology*. 2021;6: 106–119.
21. Spearman CW, Andersson MI, Bright B, et al. A new approach to prevent, diagnose, and treat hepatitis B in Africa. *BMC Global Public Health*. 2023;1:24.
22. Vinikoor MJ, Sinkala E, Kanunga A, Muchimba M, Zanolini A, Saag M. *Eligibility for Hepatitis B Antiviral Therapy Among Adults in the General Population in Zambia*. vol. 15. 2020, e0227041.
23. Abera H, Desalegn H, Berhe N, et al. *Early Experiences from One of the First Treatment Programs for Chronic Hepatitis B in Sub-saharan Africa*. vol. 17. 2017:438.
24. Iloeje UH, Yang HI, Su J, Jen CL, You SL, Chen CJ. Predicting cirrhosis risk based on the level of circulating hepatitis B viral load. *Gastroenterology*. 2006;130:678–686.
25. Sarin SK, Kumar M, Lau GK, et al. Asian-Pacific clinical practice guidelines on the management of hepatitis B: a 2015 update. *Hepatology Int*. 2016;10:1–98.
26. Terrault NA, Lok ASF, McMahon BJ, et al. Update on prevention, diagnosis, and treatment of chronic hepatitis B: AASLD 2018 hepatitis B guidance. *Hepatology*. 2018;67:1560–1599.
27. EASL 2017. Clinical Practice Guidelines on the management of hepatitis B virus infection. *J Hepatol*. 2017;67:370–398.
28. Desalegn H, Orlén SMS, Abera H, et al. *Five-year Results of a Treatment Program for Chronic Hepatitis B in Ethiopia*. vol. 21. 2023:373.
29. Ndow G, Vo-Quang E, Shimakawa Y, et al. Clinical characteristics and outcomes of patients with cirrhosis and hepatocellular carcinoma in the Gambia, west Africa: a prospective cohort study. *Lancet Global Health*. 2023;11:e1383–e1392.
30. Sow A, Lemoine M, Toure PS, et al. HBV continuum of care using community- and hospital-based screening interventions in Senegal: results from the PROLIFICA programme. *JHEP reports : innovat Hepatol*. 2022;4, 100533.
31. Somé EN, Kaboré J, Kaboré C, et al. BurkinaFaso and the global goal of eliminating Hepatitis B virus By 2030. *Adv Pub Health Commun Tropical Med*. 2022;2022(2):1–5.
32. Nankya-Mutyoba J, Apica BS, Otekat G, et al. Hepatitis C in Uganda: identification of infected blood donors for micro-elimination. *J Virus Eradication*. 2021;7, 100041.
33. Al-Ahmari TS, Alotaibi AF, Aljasser AI, Aljasser AI, Eldaw AM, Abd-Ellatif EE. The effectiveness and safety of direct-acting antivirals in the treatment of hepatitis C virus in Saudi arabia: a nationwide study based on the Saudi ministry of health surveillance data from 2017 to 2021. *Cureus*. 2023;15, e42780.
34. Maqsood Q, Sumrin A, Iqbal M, Younas S. *Hepatitis C virus/Hepatitis B Virus Coinfection: Current Prospectives*. vol. 28. 2023, 13596535231189643.
35. *Global Status Report on Alcohol and Health and Treatment of Substance Use Disorders*. Geneva: World Health Organization; 2024. Licence: CC BY-NC-SA 3.0 IGO.
36. Li Y, Chen A, Wang H, et al. Treatment adherence to nucleos(t)ide analogs in Chinese patients with hepatitis B virus-related hepatocellular carcinoma: a single-center cross-sectional study. *Patient Prefer Adherence*. 2021;15:1729–1738.
37. Marchese V, Beltrame A, Angheben A, Marocco S, Gaeta GB, Bisoffi Z. The impact of schistosomiasis co-infection in the presentation of viral hepatitis B in migrants: an observational study in non-endemic area. *Trav Med Infect Dis*. 2020;35, 101467.
38. Gunda DW, Mtui EF, Kilonzo SB, Kidenya BR, Mazigo HD. *Schistosoma mansoni* and hepatitis B co-infection among adult patients. *J Microbiol Infect Dis*. 2020;10(3): 136–143. <https://doi.org/10.5799/jmid.790280>.