

Health-Related Quality of Life in Adults with Hepatitis B in Sub-Saharan Africa: The Added Burden of HIV Co-infection

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Abstract

Background

Chronic hepatitis B (CHB) affects an estimated 82 million people in sub-Saharan Africa (SSA), where HIV co-infection is common and accelerates liver-related complications. While the clinical outcomes of HBV and HIV/HBV co-infection have been well described in SSA, health-related quality of life (HRQoL) remains less well characterized, particularly among individuals at different stages of infection and treatment exposure.

Methods

We conducted a cross-sectional analysis of baseline data from a longitudinal observational cohort of adults with HBV, with and without HIV, enrolled at five H2Net Consortium sites in Nigeria, Tanzania, and Mali. Participants were categorized into four groups: HBV mono-infection on treatment (HBV-OT), HBV mono-infection not on treatment (HBV-NOT), HIV/HBV co-infection on treatment (HIV/HBV-OT), and HIV/HBV co-infection treatment-naïve (HIV/HBV-TN). HRQoL was assessed using the SF-36 Health Survey and scored according to RAND guidelines. Multivariable linear regression was used to evaluate associations between HRQoL domains and demographic, clinical, and disease-related factors.

Results

Among 884 participants (41% HBV-OT, 33% HBV-NOT, 23% HIV/HBV-OT, 3% HIV/HBV-TN), the mean overall HRQoL score was 77.8 (SD 16.9). HRQoL was highest among participants with HBV-NOT [80.56 (SD 14.67)] and lowest among HIV/HBV-TN [59.38 (SD 23.67)] ($p < 0.01$). Across all HRQoL domains, participants with HIV/HBV co-infection (-TN and -OT combined) reported significantly lower scores compared with those with HBV alone. Energy was the most impaired domain across all groups. In multivariable analyses, HIV/HBV co-infection, whether -TN or -OT, was independently associated with lower overall HRQoL and lower scores across all HRQoL domains. Higher liver fibrosis scores, greater comorbidity burden, and older age were also associated with lower overall HRQoL scores and select HRQoL domains.

Conclusions

HRQoL impairments, particularly related to energy, emotional wellbeing, and functional limitations, are common among adults with HBV in SSA and are most pronounced in those with HIV/HBV co-infection. These impairments are not fully captured by clinical or virologic markers alone, underscoring the need for integrated care models that address psychosocial and functional health alongside antiviral treatment, particularly among those with HIV/HBV co-infection.

Background

An estimated 82 million people are living with chronic hepatitis B (CHB) infection in sub-Saharan Africa (SSA), accounting for a quarter of all global infections.¹ Nigeria, Mali, and Tanzania are some of the highest affected areas with CHB prevalence rates in the general population ranging from 5.2–14%.^{2–4} Due to similar routes of transmission, HIV is also very common among persons with CHB in these regions with prevalence rates averaging 8%.^{5,6} Complications related to CHB, such as cirrhosis and hepatocellular carcinoma (HCC), remain highly prevalent in SSA, reflecting persistent gaps in diagnosis, access to antiviral therapy, and long-term clinical care.^{7,8} Among persons with HIV/HBV co-infection, the development of liver-related complications is further accelerated due to a combination of HIV-related immune dysfunction and enhanced HBV replication.⁹ HCC, one of the most feared liver-related complications, affects approximately 46,000 individuals per year in West Africa, more than half of whom have CHB.^{10,11}

Despite the substantial burden of hepatitis B virus (HBV) and its associated complications in SSA, HBV remains poorly characterized in these settings, particularly among people co-infected with HIV receiving long-term HBV-active antiretroviral therapy (ART) and among individuals with HBV mono-infection, who are not routinely sustained in care.^{12,13} Long-term health outcomes including patient-centered outcomes, also remain poorly understood, limiting the ability to inform comprehensive models of care.

Health-related quality of life (HRQoL) is emerging as an important outcome in HBV infection although remains relatively understudied both in high-income countries and in regions where HBV is endemic. Defined as an individual's perceived physical, mental, and social wellbeing as affected by health status and disease, HRQoL captures the broader impact of HBV beyond traditional clinical measures, including physical functioning, emotional wellbeing, social participation, and mental health.^{14,15} Measuring HRQoL is particularly critical for persons with HBV, especially the large majority living with asymptomatic disease, who face psychological stress and physical symptoms like fatigue, which are often overlooked.

Several factors have been shown to affect HRQoL in persons with HBV. Clinical features including advanced stage of liver disease and fatigue and complexities of treatment can negatively impact well-being.^{14, 16,17} Psychological distress manifested through high rates of depression and anxiety has also been reported among persons with HBV, which can further reduce both mental and physical health.¹⁸ Social factors such as stigma, social isolation, economic constraints, and concerns about long-term health and prognosis can negatively impact emotional and social functioning.^{19,20} Finally, barriers at the health system level, including difficulties accessing care due to limited availability or financial constraints, also contribute to lower HRQoL, a concern that is particularly relevant in SSA, where significant gaps in healthcare access exist.²¹

Although HRQoL has been extensively studied in persons with HIV, the impact of HBV, particularly in the context of HIV co-infection, is poorly understood. Co-infected individuals may experience a “double

burden” of stigma, depression, increased morbidity, and more complex treatment regimens, all of which can cause physical, emotional and social limitations and perceived health.^{22,23} The lack of data underscores the need for further research into HRQoL and its associated factors in persons with HBV, even among persons with asymptomatic disease, who may still carry a significant psychosocial burden.

In this study, we characterized the clinical, laboratory, and sociodemographic profiles of adults with chronic HBV with and without HIV across multiple sites in Africa and assessed their HRQoL by treatment and co-infection status to better understand the clinical and psychosocial burden of HBV and HIV/HBV co-infection in this population.

Methods

Study design and population

We conducted a cross-sectional analysis of baseline data from a longitudinal observational cohort study of adults with chronic HBV with and without HIV established at five H2Net Consortium sites in Nigeria, Tanzania and Mali. The H2Net Consortium is a collaboration between Northwestern University, US; the University of Jos, University of Lagos, and University of Ibadan in Nigeria; Muhimbili National Hospital, Tanzania; and the University of Sciences, Techniques and Technologies of Bamako, Mali. Established in 2023, this collaborative conducts research and implements activities that address critical gaps in HBV, with a focus on improving clinical outcomes, strengthening HBV care delivery, and advancing translational science to support HBV elimination and future cure strategies in Africa.

Participants in the H2Net observational study were enrolled into one of four cohorts with the following inclusion criteria: **Cohort 1** HBV mono-infected on treatment (HBV-OT): (i) HBsAg seropositive; (ii) HIV seronegative; (iii) ≥ 18 years of age; (iv) receiving antiviral therapy for at least 1 month; (v) intending to stay in the region for at least 36 months; (vi) no history of decompensated liver disease, or HCC. **Cohort 2** HBV mono-infected not on treatment (HBV-NOT): Cohort 1 inclusion criteria but not receiving antiviral therapy. **Cohort 3** HIV-HBV co-infected on treatment (HIV/HBV-OT): (i) HIV and HBsAg seropositive; (ii) ≥ 18 years of age; (iii) receiving ART at least 1 month; (iv) intending to stay in the region for at least 36 months; (v) no history of decompensated liver disease, or HCC. **Cohort 4** HIV-HBV co-infected treatment naïve (HIV-HBV-TN): Cohort 3 inclusion criteria but not yet initiated ART or initiated ART ≤ 1 month prior to enrollment. Participants not able to provide consent and/or not meeting the inclusion criteria for each cohort were excluded.

Standards of care

Participants with HBV mono-infection and HIV/HBV co-infection were recruited sequentially from Hepatology and HIV clinics, respectively at Jos University Teaching Hospital (JUTH), Lagos University Teaching Hospital (LUTH) and University College Hospital (UCH) in Nigeria, Muhimbili National Hospital (MNH), Tanzania and Point G University Hospital, Mali. Hepatology clinics at participating H2Net sites

provide care to about 400–1000 persons with HBV. Approximately 25–70% are receiving antivirals. Persons with HBV mono-infection are typically seen every 6–12 months in Hepatology clinics depending on whether they are on treatment. Management of participants with HBV mono-infection at all H2Net sites follows WHO 2024 HBV treatment guidelines and national guidelines.^{24, 25} Although HBV viral loads, monitoring labs and transient elastography (TE) at H2Net sites are largely available in routine care, patients are required to pay for these studies. Tenofovir disoproxil fumarate (TDF), or tenofovir alafenamide (TAF) are recommended for participants who meet treatment eligibility. In Nigeria, entecavir is also available. In Tanzania, TDF is provided free of charge for persons with HBV. Routine counselling and education on HBV disease for patients and families, education on healthy lifestyles (including alcohol abstinence) and the importance of treatment adherence is provided at all sites. HIV clinics at participating H2Net sites provide care to about 500–2000 persons with HIV/HBV. Persons with HIV/HBV co-infection are managed according to WHO HIV treatment guidelines.^{26,27} All persons with HIV/HBV co-infection are initiated on ART after diagnosis, regardless of CD4 count, using a regimen that contains at least two agents active against HBV (TDF plus lamivudine [3TC] or emtricitabine [FTC]). Participants have access to routine HIV VL monitoring every 12 months. HBV DNA is recommended in persons with HIV/HBV co-infection every 12 months at all sites but is not free and therefore typically not offered routinely. Persons with HIV/HBV are followed every 3–6 months in the clinics depending on level of adherence and HIV virologic suppression. Each H2Net site is equipped with comprehensive laboratory infrastructure, including automated hematology and clinical chemistry analyzers, molecular PCR platforms, serologic testing capabilities, and validated cold-chain systems for the storage of blood products and archived specimens.

Data collection and management

H2Net study visits are conducted at baseline and every 6 months; the current analysis includes only data collected at the baseline visit. At enrollment, each participant undergoes a structured interview and physical examination, with collection of socio-demographic and clinical information, including HBV risk factors, medical and social history, anti(retro)viral and other medication use. Laboratory testing done at each study visit includes HBV serologic markers (HBsAg, anti-HBs, HBeAg, anti-HBe, and anti-HBc), hepatitis C virus (HCV) antibody and RNA (baseline visit only), HIV RNA viral load, complete blood count (including platelets); comprehensive metabolic panel (including urea, creatinine, ALT, and AST). TE and abdominal ultrasound are performed at baseline to assess liver fibrosis and structural abnormalities. The aspartate aminotransferase-to-platelet ratio index (APRI) was calculated for all participants at the Mali site, where TE is not available. TE, ultrasound and laboratory tests for study participants are all funded by the study. Participants also complete HRQoL (primary outcome) questionnaires using Short Form–36 Health Survey (SF-36) and scored in accordance with the RAND SF-36 scoring guidelines.²⁸

All study data are collected using standardized case report forms (CRFs) and directly entered into a secure Research Electronic Data Capture (REDCap) database hosted on the UCH, Ibadan server. Regular automated data quality checks are run to identify missing values, inconsistencies, or outliers. All data is

stored on secure servers with encrypted connections. Access to the database is password-protected. Participant identifiers were stored separately from study data; de-identified unique codes were used for analysis. Cleaned datasets were exported from REDCap in standard formats (CSV, Stata, R, or SAS) for statistical analysis.

Data analysis

Baseline sociodemographic and clinical characteristics were analyzed using descriptive statistics and compared across recruitment groups. For HRQoL measures, each survey item was transformed to a 0–100 scale, with higher scores indicating more favorable health status. Items within individual domains (physical functioning, role limitations due to physical health, role limitations due to emotional problems, pain, general health, energy/fatigue, social functioning, and emotional well-being) were averaged to generate domain-specific scores. Participants' overall HRQoL scores were calculated by averaging across all individual domain scores.²⁸

To enable comparison across recruitment sites, domain-specific and overall HRQoL scores were standardized using z-scores and subsequently reconverted to a 0–100 scale. Descriptive statistics were generated for all HRQoL domains and results were compared across recruitment groups. Overall HRQoL was also assessed via multivariate linear regression in relation to liver stiffness (measured by a binary composite variable where significant fibrosis and above was defined as TE score ≥ 7.5 kPa for sites UCH, JUTH, LUTH, and MNH; or APRI ≥ 1.5 for Point G Hospital, Mali), having ≥ 1 comorbid condition, age, sex, recruitment site, and recruitment group. All analyses were completed in Stata 18.0. Statistical significance was assessed at an alpha value of 0.05.

Ethical Considerations

The study protocol was reviewed and approved by the Institutional Review Boards (IRBs)/Ethics Committees of all participating institutions and by relevant national regulatory authorities (National Institute of Medical Research, Tanzania). Written informed consent was obtained from all participants prior to enrollment. All study procedures adhered to the ethical principles outlined in the Declaration of Helsinki and followed applicable local and international guidelines for research involving human subjects. Participant confidentiality was strictly maintained using unique study identifiers and secure, password-protected databases.

Results

Baseline characteristics

884 participants [HBV-OT 366 (41%); HBV-NOT 290 (33%); HIV/HBV-OT 200 (23%) HIV/HBV-TN 28 (3%)] were included in the analysis. Mean (SD) age of all participants was 42 (12.11). Approximately half of all HBV participants and HIV/HBV-TN were male whereas over two-thirds of HIV/HBV-OT were female.

Tertiary education was higher among participants with HBV compared to participants with HIV/HBV ($p < 0.01$). Over 90% of all participants were HBeAg negative. Among participants with HIV/HBV and HBV-OT, the duration of anti(retro)viral therapy was significantly longer in HIV/HBV-OT [123 (182)] vs. HBV-OT [49 (76)] months respectively; ($p < 0.01$). The majority (90%) HBV-OT were receiving TDF while 93% of HIV/HBV-OT were receiving dual HBV-active ART. HBV DNA levels were undetectable (< 20 IU/mL) in only half of HBV-OT and HIV/HBV-OT participants. Mean (SD) TE scores overall were 7.58kPa (10.39) with the highest 8.65kPa (10.1) and lowest 5.95kPa (3.39) scores in HBV-OT and -NOT respectively ($p = 0.04$) (4/5 sites). Mean ALT levels did not differ significantly between groups however, AST levels were significantly higher among HIV/HBV TN [60 (56)] vs. other participants ($p = 0.01$). [Table 1]

Table 1. Participant characteristics by cohort						
	HBV-OT	HBV-NOT	HIV/HBV-OT	HIV/HBV-TN	Total	p
N	366 (41.4%)	290 (32.8%)	200 (22.6%)	28 (3.2%)	884 (100.0%)	
Age (mean, SD)	42.15 (12.35)	38.64 (11.16)	47.91 (11.11)	42.59 (10.80)	42.29 (12.11)	< 0.001
Sex (% male)	59.7%	49.3%	33.3%	51.9%	50.1%	< 0.001
BMI (mean, SD)	25.81 (5.07)	25.94 (6.87)	25.27 (5.74)	22.62 (4.23)	25.64 (5.87)	0.039
Education						
None	10 (2.8%)	18 (6.2%)	10 (5.2%)	3 (11.1%)	41 (4.7%)	< 0.001
Primary	32 (8.8%)	15 (5.2%)	39 (20.1%)	4 (14.8%)	90 (10.3%)	
Secondary	73 (20.2%)	58 (20.0%)	74 (38.1%)	13 (48.1%)	218 (25.0%)	
Tertiary	247 (68.2%)	199 (68.6%)	71 (36.6%)	7 (25.9%)	524 (60.0%)	
≥ 1 comorbid condition^a	87 (24.2%)	56 (19.4%)	60 (31.1%)	8 (29.6%)	211 (24.3%)	0.030
≥ 2 symptoms^b	43 (11.9%)	35 (12.2%)	35 (18.2%)	14 (51.9%)	127 (14.7%)	< 0.001
Uses tobacco	4 (1.1%)	11 (3.8%)	9 (4.7%)	4 (15.4%)	28 (3.2%)	< 0.001
Uses alcohol	35 (9.7%)	33 (11.5%)	38 (19.8%)	8 (30.8%)	114 (13.2%)	< 0.001
ALT (IU/mL)	40.18 (90.90)	29.81 (47.23)	31.87 (75.99)	35.95 (50.18)	34.77 (74.46)	0.372
AST (IU/mL)	41.96 (68.27)	31.16 (24.01)	40.04 (38.64)	60.21 (56.29)	38.26 (50.66)	0.013
Platelets x10⁹	217.28 (94.68)	225.37 (78.33)	235.36 (104.84)	219.06 (122.50)	223.95 (92.83)	0.208
Fibroscan™, kPa (mean, SD)	8.65 (10.05)	5.95 (3.39)	7.85 (16.22)	6.70 (2.53)	7.58 (10.39)	0.044
Fibroscan, kPa						

Table 1. Participant characteristics by cohort						
	HBV-OT	HBV-NOT	HIV/HBV-OT	HIV/HBV-TN	Total	p
< 7.5	203 (72.8%)	162 (80.6%)	111 (78.7%)	7 (63.6%)	483 (76.4%)	0.002
≥ 7.5 < 12.5	42 (15.1%)	33 (16.4%)	24 (17.0%)	4 (36.4%)	103 (16.3%)	
≥ 12.5	34 (12.2%)	6 (3.0%)	6 (4.3%)	0 (0.0%)	46 (7.3%)	
APRI (mean, SD)^c	0.64 (1.57)	0.35 (0.24)	0.91 (2.43)	0.61 (0.44)	0.54 (1.31)	0.153
HBV DNA (IU/mL)						
< 20	162 (52.4%)	90 (37.2%)	95 (64.6%)	8 (50.0%)	355 (49.7%)	< 0.001
≥ 20 < 2000	98 (31.7%)	110 (45.5%)	40 (27.2%)	1 (6.2%)	249 (34.9%)	
≥ 2000	49 (15.8%)	42 (17.3%)	12 (8.2%)	7 (43.8%)	110 (15.4%)	
HBeAg positive	22 (7.6%)	16 (6.4%)	10 (8.0%)	1 (5.6%)	49 (7.2%)	0.917
Anti-HCV positive	14 (5.4%)	11 (4.8%)	4 (3.4%)	1 (5.3%)	30 (4.8%)	0.855
Hemoglobin (g/dL)	13.60 (2.68)	13.82 (7.54)	14.68 (33.97)	10.56 (2.29)	13.83 (16.55)	0.728
HIV RNA < 20 copies/mL	-	-	26 (57.5%)	-	26 (57.5%)	
Time on treatment (months; mean, SD)	39.23 (51.27)	-	123.07 (181.55)	-	49.27 (75.61)	0.000
HBV Regimen^d						
Tenofovir (AF/DF)	299 (89.0%)	-	-		299 (89.0%)	
Entecavir	5 (1.5%)	-	-		5 (1.5%)	
3TC	1 (0.3%)				1 (0.3%)	
Tenofovir/3TC	3 (0.9%)				3 (0.9%)	
Other	28 (8.3%)				28 (8.3%)	
HIV Regimen^e						

Table 1. Participant characteristics by cohort						
	HBV-OT	HBV-NOT	HIV/HBV-OT	HIV/HBV-TN	Total	p
TDV/3TC/EFV	-	-	16 (8.7%)		16 (8.7%)	
TDV/3TC/DTG	-	-	157 (85.3%)		157 (85.3%)	
Other	-	-	11 (6.0%)		11 (6.0%)	
^aComorbidities: known chronic Hepatitis C, chronic kidney disease (GFR < 60 for ≥ 3 mo), renal replacement therapy, coronary artery disease, hyperlipidemia, obesity, chronic lung disease/condition, diabetes mellitus, hypertension, malignancy ^bSymptoms: jaundice, anorexia, fever, abdominal swelling, abdominal pain, irrational talk, vomiting blood, cough, difficulty breathing, memory loss, melaena, hematochezia, vomiting, diarrhea, decreased urination, altered mental status/confusion, weight loss, weakness, leg swelling ^c USTTB site only ^dOther HBV Regimen: Tenofovir plus emtricitabine (n = 28) ^eOther HIV Regimen: Tenofovir/Lamivudine/Atazanavir (n = 6), tenofovir/emtricitabine/darunavir/ritonavir/dolutegravir (n = 1), abacavir/lamivudine/dolutegravir (n = 1), abacavir, bictegravir, atazanavir (n = 1), unspecified (n = 2)						

Health-Related Quality of Life Scores in HBV and HIV/HBV participants by treatment status

Mean (SD) scores in HRQoL overall were 77.75 (SD 16.86). HRQoL scores were highest in HBV-OT [79.13 (15.42)] and HBV-NOT [80.56 (14.67)] and lowest in HIV/HBV-TN [59.38 (23.67)] ($p < 0.01$ for between group differences). Participants with HIV/HBV (both -OT and -TN) scored consistently lower across all HRQoL domains of physical wellbeing, physical limitation, emotional limitations, emotional and social wellbeing, pain and general health compared to those with HBV (p 's all < 0.01). Across all participant groups, the highest scores were observed in physical (69.4–92.2) and social wellbeing (68.75–91.70) and pain (75.65–86.91), whereas the lowest scores were reported in energy (55.37–67.90). [Figure 1a-d, Table 2]

Table 2. Overall and domain specific Health-Related Quality of Life Scores						
	HBV-OT	HBV-NOT	HIV/HBV-OT	HIV/HBV-NT	Total	p
Overall score	79.13 (15.42)	80.56 (14.67)	73.66 (19.07)	59.38 (23.67)	77.75 (16.86)	<0.01
Physical wellbeing	91.55 (18.19)	92.20 (17.07)	80.63 (27.08)	69.44 (36.86)	88.74 (21.60)	<0.01
Physical Limitations	78.11 (38.67)	80.44 (37.43)	67.31 (44.00)	27.78 (44.04)	74.97 (40.79)	<0.01
Emotional Limitations	76.84 (39.87)	75.23 (41.13)	63.19 (46.55)	37.04 (49.21)	72.11 (42.85)	<0.01
Energy	67.90 (13.391)	67.47 (12.98)	63.87 (14.68)	55.37 (20.43)	66.46 (14.03)	<0.01
Emotional wellbeing	74.48 (12.94)	72.92 (13.11)	71.85 (13.62)	59.85 (16.73)	72.92 (13.50)	<0.01
Social wellbeing	91.42 (17.87)	91.70 (18.79)	84.86 (25.79)	68.75 (32.83)	89.41 (21.14)	<0.01
Pain	86.91 (19.92)	86.48 (19.84)	81.35 (22.12)	75.65 (30.34)	85.22 (20.92)	<0.01
General health	73.41 (19.24)	73.95 (18.85)	74.07 (20.36)	59.44 (21.94)	73.29 (19.57)	<0.01

Multivariable Analysis of Factors Associated with HRQoL

After adjusting for age, sex, comorbidities, fibrosis score and site, both HIV/HBV -OT and -TN compared with HBV -OT, were inversely associated with overall HRQoL scores, indicating significantly lower perceived quality of life among participants with HIV/HBV co-infection. Similar trends were observed across each of the specific HRQoL domains with inverse associations observed between HIV/HBV-OT and -TN and physical wellbeing, physical and emotional limitations ($p = 0.13$ for HIV/HBV-OT, physical limitations), energy, emotional and social wellbeing and pain ($p = 0.27$ for HIV/HBV-TN, pain). Only HIV/HBV- TN was associated with significantly lower scores in the general health domain. Additionally, inverse associations were also observed between significant fibrosis or above and overall HRQoL (coefficient -4.48 , $p < 0.01$), energy (-3.91 , $p < 0.01$) emotional wellbeing (-3.57 , $p < 0.01$) and general health (coefficient -7.46 , $p < 0.01$). Older age was inversely associated with overall HRQoL, physical wellness and physical and emotional limitation. In contrast, older age was positively associated with social wellbeing. [Table 3]

Table 3
Multivariable Analysis of Factors Associated with Overall HRQoL Score

Age	Overall	95% CI	Physical Wellbeing	95% CI	Physical Limitations	95% CI
	-0.12*	-0.22, -0.01	-0.20**	-0.33, -0.07	-0.45**	-0.71, -0.19
Sex	0.89	-1.42, 3.19	0.42	-2.54, 3.37	4.35	-1.52, 10.21
Site	-0.53	-1.32, 0.23	-0.96	-1.95, 0.04	-0.88	-2.86, 1.10
Significant fibrosis or above ^a	-4.48**	-7.49, -1.47	-2.22	-6.10, 1.67	-1.12	-8.83, 6.60
≥ 1 comorbidity	-3.10*	-5.89, -0.31	-1.76	-5.34, 1.82	-5.53	-12.66, 1.59
Group (vs. HBV - OT)						
HBV-NOT	-0.68	-3.26, 1.91	-0.49	-3.82, 2.82	-1.47	-8.08, 5.13
HIV/HBV -OT	-4.71**	-7.80, -1.62	-8.51**	-12.48, -4.54	-6.11	-13.98, 1.76
HIV/HBV -TN	-18.31**	-26.14, -10.48	-11.70*	-21.86, -1.54	-42.33**	-62.53, -22.13

Age	Emotional Limitations	95% CI	Energy	95% CI	Emotional Wellbeing	95% CI
Sex	-0.30 *	-0.58, -0.02	-0.05	-0.14, 0.04	0.05	-0.04, 0.13
Site	6.12	-0.12, 12.46	0.38	-1.66, 2.41	-0.05	-2.02, 1.93
Significant fibrosis or above ^a	-0.92	-3.04, 1.19	-0.26	-0.95, 0.42	-0.96**	-1.62, -0.29
≥ 1 comorbidity	-5.29	-13.57, 3.00	-3.91**	-6.59, -1.23	-3.57**	-6.17, -0.97
Group (vs. HBV OT)	-5.35	-12.98, 2.27	0.92	-1.54, 3.38	0.63	-1.76, 3.02
HBV - NOT						
HIV/HBV -OT	-4.20	-11.29, 2.87	-2.20	-4.49, 0.10	-2.23*	-4.45, -0.01
HIV/HBV -TN	-10.50*	-18.94, -2.05	-3.88**	-6.61, -1.15	-3.20*	-5.85, -0.55
	-30.39**	-52.08, -8.70	-11.01**	-18.00, -4.03	-15.88**	-22.68, -9.09

Age	Social Wellbeing	95% CI	Pain	95% CI	General Health	95% CI
	0.14*	0.01, 0.27	-0.10	-0.23, 0.03	0.06	-0.07, 0.19
Sex	1.38	-1.51, 4.26	1.65	-1.29, 4.59	1.34	-1.51, 4.18
Site	-0.33	-1.30, 0.64	-1.52**	-2.51, -0.53	-1.32**	-2.27, -0.36
Significant fibrosis or above ^a	-3.09	-6.89, 0.70	-1.03	-4.90, 2.85	-7.46**	-11.19, -3.72
≥ 1 comorbidity	-1.86	-5.36, 1.65	-5.19**	-8.75, -1.62	-3.13	-6.57, 0.31
Group (vs. HBV OT)						
HBV - NOT	-0.09	-3.34, 3.16	-1.47	-4.78, 1.84	-0.93	-4.14, 2.27
HIV/HBV -OT	-4.21*	-8.10, -0.33	-4.45*	-8.40, -0.51	-0.18	-2.99, 3.63
HIV/HBV -TN	-17.33**	-27.26, -7.41	-5.68	-15.82, 4.46	-15.45**	-25.23, -5.67
^s Significant fibrosis or above -TE score of ≥ 7.5kPa (JUTH, LUTH, UCH, MNH); APRI ≥ 1.5 (USTTB)						
*p < 0.05						
**p < 0.01						

Discussion

We report findings from one of the few studies in SSA that characterize HRQoL among individuals with HBV, both with and without HIV co-infection. Our analysis identified important differences in baseline clinical and laboratory health indicators, as well as HRQoL, according to HIV co-infection and treatment status.

Similar to other observational cohorts of HBV and HIV/HBV co-infection, our study participants were predominantly young, with a high prevalence of HBeAg-negative infection^{29–31}. Among HBV-NOT participants, HBV disease activity was relatively mild. Most had low HBV viral loads (83% <2000 IU/mL) and low fibrosis scores, consistent with inactive or minimally active disease. In contrast, HBV-OT participants had the highest fibrosis scores, with 12% of those who had TE categorized as having cirrhosis, supporting the likelihood that treatment initiation in this group was driven by more advanced liver disease. HIV/HBV-TN participants had the highest burden of comorbidities and exhibited markers of greater systemic and hepatic disease activity, including anemia, elevated AST levels, and higher HBV

viral loads, as expected. Higher rates of liver disease and more advanced immunosuppression in co-infected persons compared to those with either HBV or HIV mono-infection have been frequently reported in other African cohorts.^{31–33}

Despite the high burden of HBV in SSA, HRQoL has rarely been assessed in persons with HBV in Africa. The few HRQoL studies that have been conducted have been limited to high-income settings and among individuals with HBV mono-infection alone.¹⁴ In our study, overall HRQoL scores among persons with HBV were relatively high and comparable to these other studies (mean scores approximately 78–80).¹⁴ HRQoL was however, significantly lower among individuals with HIV/HBV co-infection compared with those with HBV mono-infection, with the lowest overall and domain-specific scores observed among HIV/HBV-TN. In multivariable analyses, both HIV/HBV co-infected groups were inversely associated with overall HRQoL and most HRQoL domains.

Across all participant groups, HRQoL scores were highest in physical wellbeing, social wellbeing, and pain domains, with lower reported scores in energy. This pattern could suggest that many participants with HBV perceive themselves as physically functional, socially integrated, and relatively free from pain, reflecting clinical stability and adaptation to their underlying disease. In contrast, low energy scores may reflect persistent fatigue, a common and under-recognized symptom in both HBV and HIV, even in the absence of advanced liver disease or uncontrolled viremia.^{34–37} Fatigue may be driven by chronic immune activation, low-grade inflammation that occurs even in the absence of elevated enzymes or symptoms, polypharmacy, or psychosocial stressors rather than by objective markers of disease severity.³⁸ In multivariable models, HIV/HBV co-infection both -TN and -OT, was associated with significantly lower scores in all four of these domains compared to HBV mono-infected participants. This finding is not unexpected and likely reflects the additional clinical and psychosocial burden associated with living with two chronic viral infections. Individuals with HIV/HBV co-infection frequently experience higher comorbidity burdens, higher rates of hospitalizations and persistent immune dysregulation despite treatment, all of which can negatively influence perceived physical health, energy levels, social wellbeing, and overall quality of life.^{39,40}

Among persons with HBV-OT, HBV-NOT, and HIV/HBV-OT, relatively high scores were also observed in emotional wellbeing and in domains reflecting physical and emotional limitations. In multivariable analyses, both HIV/HBV-TN and -OT groups were again associated with significantly lower scores in emotional wellbeing and emotional limitations compared to HBV-mono-infected. Only HIV/HBV-TN status was associated with lower physical limitation scores. HIV has been frequently shown to be associated with higher rates of depression, anxiety, stigma, and social vulnerability, all of which can negatively affect emotional wellbeing independent of virologic control.⁴¹ Living with two chronic viral infections may contribute to heightened concerns about long-term health, stigma, and treatment complexity, which can negatively affect emotional wellbeing and perceived functional capacity.^{42,43} The strong association between HIV/HBV-TN status and lower physical limitation scores may also reflect the complications of untreated HIV such as anemia and other comorbidities were much more prevalent in

our HIV/HBV-TN group and likely contributed to poorer functioning. Interestingly, compared with HBV-OT, HBV-NOT was also associated with lower emotional wellbeing.

The lower emotional wellbeing observed among HBV-NOT compared with HBV-OT may reflect uncertainty about disease progression or perceived lack of active management, anxiety regarding monitoring, eligibility for treatment, or future liver complications.¹⁸ However, this relationship requires further investigation in larger qualitative studies of untreated chronic HBV. Together, these findings highlight that psychological and functional aspects of health-related quality of life may be influenced not only by clinical disease status but also by treatment engagement, perceived disease control, and the broader psychosocial context of living with chronic viral infections.

Other important predictors of HRQoL in our cohort, beyond coinfection status, were fibrosis stage and age. The finding of an inverse association between significant fibrosis or greater and overall HRQoL as well as energy, emotional wellbeing, and general health domains is consistent with other studies.^{14,44} Increasing fibrosis severity has been associated with greater symptom burden, systemic inflammation, and heightened health-related anxiety, all of which can negatively influence perceived quality of life and domains closely related to overall health perception.⁴⁵ The inverse association between age and overall HRQoL, physical wellbeing, physical limitation, and emotional limitation scores and positive association with social wellbeing has also been previously reported and likely reflects the cumulative effects of aging, including increasing comorbidities, reduced physical functioning, and greater health-related limitations that may affect both physical and emotional domains.⁴⁶ In contrast, improved social wellbeing among older participants may reflect greater social stability, more established support networks, and potentially greater psychological adaptation to living with chronic disease over time.^{47,48}

Limitations

This study has some limitations. First, the cross-sectional analysis precludes causal inferences between HBV/HIV status and HRQoL or clinical outcomes. Longitudinal analyses are planned which will better assess changes in HRQoL over time and allow for evaluation of how these changes relate to clinical outcomes. Second, participants were primarily recruited from healthcare facilities, which may overrepresent individuals engaged in care and underrepresent those not accessing services, limiting generalizability. Third, HRQoL and psychosocial measures were self-reported and may be subject to recall or social desirability bias. Fourth, variability in healthcare infrastructure, treatment availability, and local practices across study sites may have influenced observed outcomes. For example, educational attainment was highest at sites in Nigeria, while nearly universal health insurance coverage and high levels of education were reported in Tanzania (data not shown). Both factors could have influenced HRQoL despite adjustment. Finally, residual confounding from unmeasured factors, such as socioeconomic status or geographic location, may have influenced our findings, and results may not fully generalize to all HBV or HIV/HBV populations in SSA, particularly in rural or underserved communities.

Conclusions

Overall, our study findings demonstrate that HRQoL impairments, particularly in energy, emotional wellbeing, and functional limitations, are not fully captured by clinical or virologic markers alone and disproportionately affect individuals with HIV/HBV co-infection. Our results underscore the importance of integrated care models that address mental health, fatigue, and functional status alongside antiviral treatment, especially in those with co-infection. Greater attention is needed for earlier identification of HBV, timely treatment initiation when indicated, and optimization of antiviral therapy to achieve sustained virologic suppression and prevent progression of liver disease, which may have important benefits not only for clinical outcomes but also for patient-reported wellbeing. Further research is needed to better understand the drivers of impaired HRQoL among people living with HBV, especially those with HIV co-infection. Culturally adapted interventions and supportive policies that address psychological, social, and physical needs are essential to improving quality of life in this population.

Abbreviations

APRI	Aminotransferase-to-platelet ratio index
AST	Aspartate aminotransferase
ART	Anti-retroviral therapy
ALT	alanine aminotransferase
CHB	Chronic Hepatitis B
HBV	Hepatitis B virus
HCV	Hepatitis C virus
HIV	Human immunodeficiency virus
HRQoL	Health-related quality of life
OT	On treatment
SSA	Sub-Saharan Africa
TE	Transient elastography
TN	

Treatment naïve

Declarations

Ethics approval and consent to participate

The study protocol was reviewed and approved by the Institutional Review Boards (IRBs)/Ethics Committees of all participating institutions and by relevant national regulatory authorities (National Institute of Medical Research, Tanzania). Written informed consent was obtained from all participants prior to enrollment. All study procedures adhered to the ethical principles outlined in the Declaration of Helsinki and followed applicable local and international guidelines for research involving human subjects. Participant confidentiality was strictly maintained through the use of unique study identifiers and secure, password-protected databases.

Clinical trial number

Not applicable

Consent for publication

Not applicable

Competing interests

The authors declare that they have no competing interests.

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Author Contribution

CH and EO conceived the study and secured funding. CH, EO, JRw, EC and PD designed the protocol. EO, JR, MD, SA and YC coordinated site implementation and enrolled study participants. MO, MSK, EU, and GO also enrolled study participants. BC performed statistical analyses. EA, TO, HA, NA and MK collected,

maintained and performed quality checks on study data. CH and EO interpreted the study results and drafted the manuscript. All authors contributed to data interpretation, critically revised the manuscript, and approved the final version.

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Data Availability

Due to the sensitive nature of HIV-related clinical data, de-identified individual participant data are not publicly available. Data may be shared in a de-identified form with qualified researchers upon reasonable request to the corresponding author with no prior approval from the institutional ethics committees.

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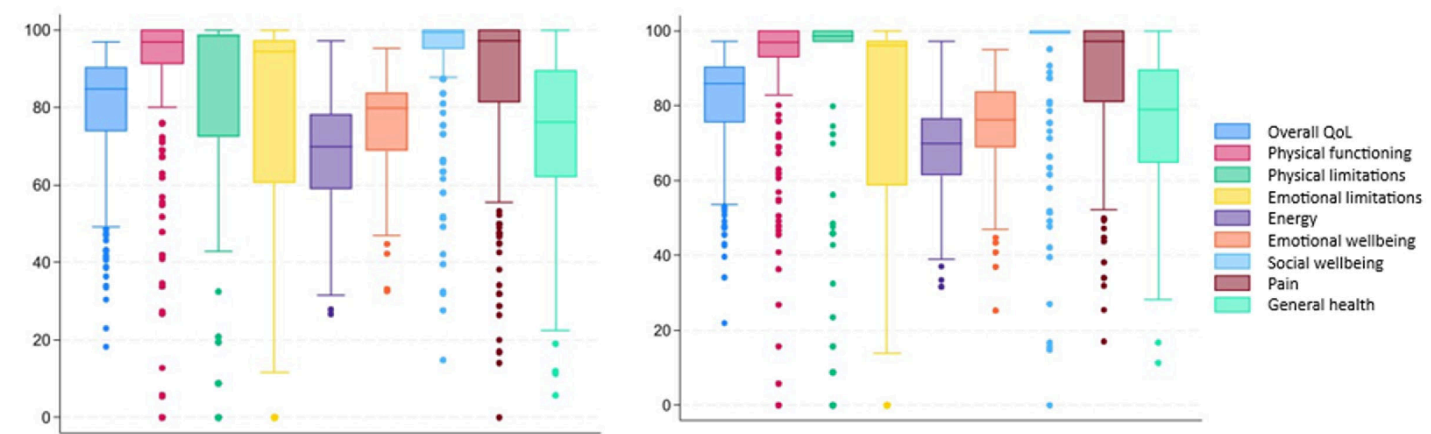
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Figures

a) HBV-OT

b) HBV-NOT



c) HIV/HBV- OT

d) HIV/HBV-NOT:

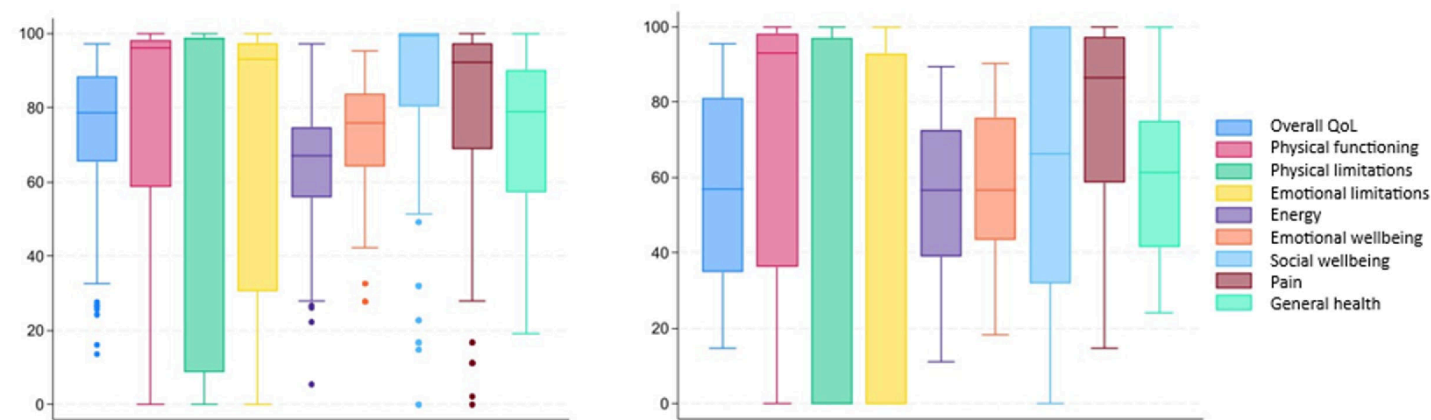


Figure 1

a-d. Overall and Domain-Specific Health-Related Quality of Life Scores by Participant Group