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Liver Fibrosis by Transient Elastography Among HIV/HBV and HBV-Mono Infected Patients on Long-Term Tenofovir Therapy in Jos, Nigeria

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Abstract

Introduction: Chronic Hepatitis B (CHB) infection both in HIV coinfection and HBV-mono infection are associated with risk of progression to chronic liver disease. Combined tenofovir cART and mono-tenofovir have improved survival in CHB patients. There is paucity of data on Transient Elastography (TE) in HIV/HBV and HBV-mono infected patients. We aimed to assess liver fibrosis using transient elastography in relation to liver function biomarkers and HBV DNA among HIV/HBV and HBV-mono infected patients on long-term antiviral therapy.

Methods: A cross-sectional study in HBV-HIV and HBV-mono infected adults patients receiving a tenofovir-containing antiretroviral and mono-tenofovir ≥12months at four selected tertiary hospitals in Jos Metropolis from February 2018 to May 2019, after obtained ethical approval from the IRBs and informed consents. The patients' HBV DNA, platelet count, hematological, biochemical parameters were assessed and liver stiffness measured by TE in kilopascals (kPa), and valid TE measurements were interpreted as: normal (F0-1 0-4), minimal fibrosis (F2 5-7.4), moderate (F3 7.5.9.4), severe fibrosis and cirrhosis (F4 ≥9.5).

Results: A total of 101 (50 HIV/HBV and 51 HBV-mono infected) were enrolled during the study period, comprising of 42.6% males and 57.4% females. The median age interquartile range (IQR); among the HIV/HBV was 40.5(36.0-45.3) and HBV-mono infected 41.0(35.0-49.0). The median Platelet count was low in HBV-mono 195 (168-257), p 0.034. The overall prevalence of severe liver fibrosis (≥ 9.5kPa) was 13/101(13.0%), and among HIV/HBV coinfected and HBV-mono infected patients was 4/50 (8.0%) and 9/51 (17.6%) respectively. The plasma HBV-DNA was <20 copies/mL in 38/50 (76.0%) HIV/HBV and in 30/51(58.8%) HBV-mono patients, 10/50(20.0%) HIV/HBV and 19/50 (37.3%) HBV-mono patients had plasma HBV-DNA of 20-20000 copies/mL. The prevalence of Severe fibrosis (≥ 9.5): in HIV/HBV was 4(8.0%), HBV-mono 9(17.6%). The overall prevalence of thrombocytopenia was 4/101(3.9%): HIV/HBV 1(2.0%) and HBV-mono 3(5.9%).

Key words: Liver fibrosis; Transient Elastography; Tenofovir; Chronic Hepatitis B virus; Nigeria

INTRODUCTION

Hepatitis B virus (HBV) infection remains a severe public health challenge worldwide, especially in sub-Saharan Africa (SSA), despite the introduction of HBV vaccination and effective anti-viral therapy to treat HBV. Though the risk of horizontal and vertical mother-to-child transmission has significantly reduced [1]. However, it is estimated that over 248 million persons are still chronically infected by HBV worldwide [2]. However, the social and economic burden remains a serious concern, but little concerted efforts have been made by policy makers and healthcare providers to improve funding, awareness and access to HBV infection management [3]. The clinical manifestation of chronic hepatitis B (CHB) vary significantly, ranging from spontaneous resolution of the infection to severe consequences, including asymptomatic phase, development of hepatic failure, cirrhosis, and end stage liver disease and or hepatocellular carcinoma (HCC) [4]. The disease progression of HBV infection is as a consequence of combined factors, including the host immune response, viral, as well as age, sex and environmental factors [5]. The individuals with CHB have a lifetime risk of severe adverse outcomes ranging from 15%–40% [6]. Early diagnosis and initiation of antiviral treatment for those that are at risk is essential to prevent the development of further clinical complications.

In Nigeria, the prevalence of HBV infection is inhomogeneous across different populations and geopolitical zones. A recent national survey reported the prevalence of hepatitis B infection to be at 12.2% [7,8]. The pooled prevalence of HBV in Nigeria from different studies carried out among adults between 2000 and 2013 was 13.6% and for children was 1.2-15.5% [9,10]. HBV prevalence in Nigeria also varied by the screening methods used; the result varied from 9 -17.5%, however, HBV infection is thus hyperendemic in Nigeria and may be one of the highest in sub-Saharan Africa. The prevalence among HIV infected and pregnant women ranged from 3-15% [9-12].

Many studies have demonstrated that liver function markers, such as, alanine aminotransferase (ALT), aspartate aminotransferase (AST) and albumin (ALB), bilirubin exhibited a marked variation in different HBV infected patients [13]. However, HBV DNA replication and levels serves a central role in maintaining persistent infection and are associated with the extent of liver damage and severity [14]. It's also important to note that intervention by early detection of hepatic fibrosis which is a pathological change caused by chronic liver damage is critical to the management of HBV infection. The early stage of hepatic fibrosis is reversible, and therefore, the prevention and control of early liver fibrosis are of great significance. Transient elastography (TE) (Fibro scan, Echosens, Paris, France) is a non-invasive technique conceived to indirectly assess liver fibrosis for measuring liver stiffness (LS) [15]. The scan is performed with an ultrasound transducer probe that produces vibrations of mild amplitude and low frequency, which induces an elastic shear wave that propagates through the liver tissue [16]. The velocity of the shear wave is directly related to liver tissue stiffness; the harder the tissue is, the faster the shear wave propagates [16]. The result is expressed as a pressure in kilopascals (kPa). The emergence of TE for detection of early liver fibrosis remains a feasible strategy to identify and prevent disease progression in CHB patients [17]. The present study investigated the liver fibrosis using transient elastography in relation to liver function biomarkers and HBV DNA among HIV/HBV and HBV -mono infected patients on long-term antiviral therapy.

METHODOLOGY

This was a cross-sectional study conducted at the Jos University Teaching Hospital (JUTH), Faith Alive Foundation Jos, Bingham University Teaching Hospital Jos, Plateau Sate Specialist Hospital HIV Treatment Center, Jos, Nigeria, after obtained Ethical approval from the Institutional Review Boards (IRBs). A written informed consent was provided by all patients. The study recruited HIV coinfected with HBV (HIV/HBV) and HBV-mono infected adults aged ≥18 years between February 2018 to May 2019, who have been on tenofovir based antiretroviral combination (HIV/HBV), and on tenofovir monotherapy (HBV-mono infected) for at least 12 months. A patient classified as HIV/HBV coinfected or HBV-mono infected if the patient was tested positive for hepatitis B surface antigen (HBsAg), We tested all patients for liver fibrosis using Transient Elastography (Fibro scan), HBV DNA, hemoglobin, neutrophil, creatinine, alanine aminotransferase (ALT), aspartate transaminase (AST) levels, platelet count, bilirubin and albumin at enrollment. Hepatitis B virus DNA was determined using the Roche COBAS® TaqMan® HBV Test (Roche Diagnostics GmbH, Mannheim, Germany) with a lower limit of detection of 10 copies/mL. At the time of HBV DNA quantification and TE testing, the HIV/HBV were on tenofovir based-ART and the HBV-mono on tenofovir mono-therapy. Plasma HIV type 1 (HIV-1) RNA was quantified by Real Time HIV-1 assay (Abbott Diagnostics, UK). All laboratory

tests were performed according to the manufacturer's specifications.

Measurement of Liver Stiffness by Transient Elastography (TE)

Transient Elastography was performed using portable equipment (Fibro scan, Ecosens, France). Valid TE measurements were interpreted as: normal (F0-1 0-4), minimal fibrosis (F2 5-7.4), moderate (F3 7.5.9.4), severe fibrosis and cirrhosis (F4 ≥9.5) (Marcellin et al 2009). Blood samples were collected at the time of TE, CD4 cell counts, full blood counts, and serum biochemistry performed in the APIN laboratory Jos University Teaching Hospital. The liver stiffness measurement in kilopascal (kPa) was performed by trained physicians by the manufacturer.

Statistical Analysis

The data obtained was analyzed using statistical package for social sciences (SPSS) version 20.2 Inc. Chicago, Illinois -USA for descriptive statistics, and continuous variables were presented as mean (standard deviation) or median (interquartile range [IQR]), as appropriate. Categorical variables were presented in number (percentage). Student t test was used in comparison of Fibrosis score value between groups. A p value of <0.05 for 2-sided test was considered to be statistically significant.

RESULTS

A total of 50 HIV/HBV and 51 HBV-mono infected were enrolled during the study period, comprising of 42.6% males and 57.4% females. The summary of the characteristics of the study population are presented in Table 1.

The median age interquartile range (IQR); among the HIV/HBV was 40.5(36.0-45.3) and HBV-mono infected 41.0(35.0-49.0). The median plasma HIV RNA was 33(10-283), CD4 was 497(314.8-659.3) in HIV/HBV coinfected. The overall prevalence of severe liver fibrosis (≥9.5kPa) 13/101(13.0%), and among HIV/HBV coinfected and HBV-mono infected patients was 4/50 (8.0%) and 9/51 (17.6%) respectively. The plasma HBV-DNA was <20 copies/mL in 38 of 50 (76.0%) HIV/HBV and in 30 of 51(58.8%) HBV-mono patients, 10/50(20.0%) HIV/HBV

Table 1: Characteristics of HIV/HBV and HBV-mono Infected Patients on Long-term Tenofovir therapy in Jos.

Characteristics	HIV-HBV Co-infection (n=50)	HBV Mono-infection (n=51)	P value
Age, y, median (IQR)	40.5 (36.0-45.3)	41.0 (35.0-49.0)	
Sex	Male 19, Female 31)	Male 24, Female 27	
HBV DNA, copies/median (IQR)	1 (1-44)	20 (1-121)	
<20	38 (76.0)	30 (58.8)	0.155
20-20000	10 (20.0)	19 (37.3)	
>20000	2 (4.0)	2 (3.9)	
Log10 HBV DNA copies/mL, median (IQR)	0 (0-1.5)	0 (0-2.1)	
Fibro scan score, kPa, categorised, No. (%)			
F0/F1 Normal (<5)	24 (48.0)	13 (25.5)	0.072
F2 Minimal fibrosis (5-7.4)	19 (38.0)	22 (43.1)	
F3 Moderate (7.5-9.4)	3 (6.0)	7 (14.0)	
F4 Severe fibrosis (≥ 9.5)	4 (8.0)	9 (17.6)	
Fibro scan score, kPa, categorised, No. (%)			
Not significant (< 9.3)	46 (92.0)	42 (82.4)	0.234†
Significant fibrosis (≥ 9.3)	4 (8.0)	9 (17.6)	
RNA viral load, median (IQR)	33 (10-283)	-	0.28
CD4 count, cells/μL, median (IQR)	497.5 (314.8-659.3)	-	0..62
Haemoglobin, g/Dl, median (IQR)	13.1 (12-14)	13 (13-14)	0.647
WBC, cells/μL, median (IQR)	6.0 (4.9-7.6)	5.9 (5-6.9)	0.067
Lymphocytes, cells/μL, median (IQR)	48 (38.0-54.5)	46 (35-50)	0.706
Neutrophil, (109/L) median (IQR)	47.5 (38.8-56.5)	41 (34-51)	0.645
Platelet (109/L), median (IQR)	259 (198.3-298.8)	195 (168-257)	0.034
Creatinine, μMol/L, median (IQR)	65.5 (55.5-76.3)	70 (57-85)	0.078
ALT, (μ/L), median (IQR)	26.1 (19.8-35.5)	27 (20-41)	0.538
AST, (μ/L), median (IQR)	28 (23.8-36.0)	27 (19-32)	0.334
Albumin, g/dL, median (IQR)	4.8 (4.5-5.0)	4.6 (4.0-4.9)	0.067
Bilirubin, mg/dL, median (IQR)	1.3 (1.2-1.5)	1.4 (1.3-1.6)	0.058
Urea, mg/dL, median (IQR)	21 (15.8-27.3)	20 (15-23)	0.235

and 19/51 (37.3%) HBV-mono patients had plasma HBV-DNA of 20-20000 copies/mL. Liver stiffness measured by Transient Elastography (Fibro scan) and score quantified in kilopascals (kPa) as F0/F1-1 0-4.9 as normal, F2 5-7.4 as minimal fibrosis, F3 7.5.9.4, as moderate fibrosis, and F4 ≥9.5 as severe fibrosis. The prevalence of Severe fibrosis (≥ 9.5): in HIV/HBV was 4(8.0%), HBV-mono 9(17.6%). Thrombocytopenia was defined as platelet count of <150 × 109/l). The overall prevalence of thrombocytopenia was 4/101(3.9%): HIV/HBV 1(2.0%) p=0.029, and HBV-mono 3(5.9%). The median HIV-RNA among the HIV/HBV was 33(10-283), and CD4 cell count was 497.5(314.8-659.3). The median lymphocytes (IQR) were low in HBV-mono 46 cells/µL and 48 cells/µL HIV/HBV. Also, the Neutrophil count was low in HBV-mono 41 (34-051), HIV/HBV 47.5 (38.8-56.5). The median Platelet count was low in HBV-mono 195 (168-257), p 034. For Fibro scan results: 3(6.0%) patients had F3, 7(14.0%) in HIV/HBV and HBV-mono, and 4(8.0%) patients had F4, while 9(17.6%) in HIV/HBV and HBV-mono respectively (Tables 1). Comparisons as regards to age category showed no significant difference between the two groups, but severe liver fibrosis was found more in 38-47 years among HIV/HBV and HBV-mono: 2(8.3%) in HIV/HBV and 4(25.0%) in HBV-mono. For sex category, the severe liver fibrosis was in females 4(12.9%) HIV/HBV, and more among females) 5(18.5%) HBV-mono. The use of alcohol was also compared among the two groups, severe liver fibrosis was more in those who answered to alcohol consumption in HBV-mono (5(19.2%%), and showed a statistically nonsignificant difference (Table 2).

On comparing patients with different liver fibrosis stages and HBV DNA, although most patients in both groups had viral loads of 20-20000 copies/mL (Table 3), with no statistically significant difference, but significant difference was observed in relation to severe liver fibrosis and thrombocytopenia in HIV/HBV patients P=0.029 (Table 4).

Table 2: Liver Stiffness measurement associated with Age categories among HIV/HBV and HBV-mono Infected Patients on Long-term Tenofovir therapy in Jos.

Age category	No. of sample	HIV-HBV				HBV			
		18-27yrs	28-37yrs	38-47yrs	>47yrs	18-27yrs	28-37yrs	38-47yrs	>47yrs
F0/F1 Normal (<5)	60 (59.4)	0 (0.0)	13 (68.4)	17 (70.8)	6 (85.7)	1 (25.0)	6 (37.5)	11 (68.8)	6 (40.0)
F2 Minimal fibrosis (5-7.4)	18 (17.8)	3 (15.8)	3 (15.8)	4 (16.7)	0 (0.0)	2 (50.0)	5 (31.3)	1 (6.3)	3 (20.0)
F3 Moderate (7.5-9.4)	10 (9.9)	2 (10.5)	2 (10.5)	1 (4.2)	0 (0.0)	0 (0.0)	4 (25.0)	0 (0.0)	3 (20.0)
F4 Severe fibrosis (≥ 9.5)	13 (12.9)	0 (0.0)	1 (5.3)	2 (8.3)	1 (14.3)	1 (25.0)	1 (6.3)	4 (25.0)	3 (20.0)
p-value		0.797				0.166			
Sex		**HIV-HBV**				**HBV-mono**			
		Male		Female		Male		Female	
F0/F1 Normal (<5)	60 (59.4)	13 (68.4)		23 (74.2)		11 (45.8)		13 (48.1)	
F2 Minimal fibrosis (5-7.4)	18 (17.8)	3 (15.8)		4 (12.9)		6 (25.0)		5 (18.5)	
F3 Moderate (7.5-9.4)	10 (9.9)	3 (15.8)		0 (0.0)		3 (12.5)		4 (14.8)	
F4 Severe fibrosis (≥ 9.5)	13 (12.9)	0		4 (12.9)		4 (16.7)		5 (18.5)	
p-value		0.058		0.953					
Alcohol Use		Yes		No		Yes		No	
F0/F1 Normal (<5)	60 (59.4)	7 (58.3)		29 (76.3)		12 (46.2)		12 (48.0)	
F2 Minimal fibrosis (5-7.4)	18 (17.8)	1 (8.3)		6 (15.8)		4 (15.4)		7 (28.0)	
F3 Moderate (7.5-9.4)	10 (9.9)	2 (16.7)		1 (2.6)		5 (19.2)		2 (8.0)	
F4 Severe fibrosis (≥ 9.5)	13 (12.9)	2 (16.7)		2 (5.3)		5 (19.2)		4 (16.0)	
p-value		0.154		0.533					

Table 3: Liver Stiffness measurement associated with HIV/HBV and HBV-mono Infected Patients on Long-term Tenofovir therapy in Jos.

Fibrosis profile	No. of sample	HIV-HBV (n=50)				HBV (n = 51)			
		< 20	20-20000	>20000	Total (%)	< 20	20-20000	>20000	Total (%)
F0/F1 Normal (<5)	60 (59.4)	30 (78.9)	5 (50.0)	1 (50.0)	36 (60.0)	14 (46.7)	9 (47.4)	1 (50.0)	24 (40.0)
F2 Minimal fibrosis (5 – 7.4)	18 (17.8)	5 (13.2)	2 (20.0	0 (0.0)	7 (38.9)	7 (23.3)	3 (15.8)	1 (50.0)	11 (61.1)
F3 Moderate (7.5 – 9.4)	10 (9.9)	1 (2.5)	2 (20.0)	0 (0.0)	3 (30.0)	4 (13.3)	3 (15.8)	0 (0.0)	7 (70.0)
F4 Severe fibrosis (≥ 9.5)	13 (12.9)	2 (5.3)	1 (10.0)	1 (50.0)	4 (30.8)	5 (16.7)	4 (21.1)	0 (0.0)	9 (69.2)
p-value		0.104				0.927			

Table 4: Liver Stiffness measurement associated with Platelet counts among HIV/HBV and HBV-mono Infected Patients on Long-term Tenofovir therapy in Jos.

Fibrosis score	No. of sample	HIV-HBV			HBV		
		Thrombocytopenia	Normal	Thrombocytosis	Thrombocytopenia	Normal	Thrombocytosis
F0/F1 Normal (<5)	60 (59.4)	0 (0.0)	35 (74.5)	1 (50.0)	1 (33.3)	23 (47.9)	0 (0.0)
F2 Minimal fibrosis (5-7.4)	18 (17.8)	0 (0.0)	6 (12.8)	1 (50.0)	1 (33.3)	10 (20.8)	0 (0.0)
F3 Moderate (7.5-9.4)	10 (9.9)	0 (0.0)	3 (6.4)	0 (0.0)	0 (0.0)	7 (14.6)	0 (0.0)
F4 Severe fibrosis (≥ 9.5)	13 (12.9)	1 (100.0)	3 (6.4)	0 (0.0)	1 (33.3)	8 (16.7)	0 (0.0)
Total	101	1	47	2	3	48	0
p-value		0.029			0.75		

DISCUSSION

Chronic hepatitis B infection mostly leads to liver disease, and the prognosis and management depends greatly on the amount and progression of liver fibrosis. The assessment of liver fibrosis by TE is considered an important factor to reliably rule out cirrhosis [18]. Liver-related decompensation and mortality are expected to rise overtime due to incidence of advanced liver fibrosis in sub-Saharan population [19]. Therefore, the correct and early evaluation of liver fibrosis is fundamental to the management of chronic liver disease and associated complications [20]. Before now, liver biopsy as an invasive method has been the gold standard, but because of its limitations, a noninvasive alternative method amongst others such as Fibro scan have been developed. Higher levels of liver stiffness measures and biochemical scores are predictive of these events during treatment in HIVHBV and HBV mono-infected patients [21].

This study presents the first analysis of liver fibrosis by Transient Elastography (Fibro scan), and associated biomarkers of liver disease and HBV DNA among HIV/HBV-coinfected and HBV-mono patients on long-term tenofovir therapy in Nigeria. However, few studies from Nigeria have assessed liver fibrosis using TE in HIV and HBV-coinfected patients, Ghana, [22] Egypt, [23] and Zambia [24].

In this study, the prevalence of liver fibrosis among HIV/HBV coinfected (8.0%), HBV-mono infected patients (17.6%) were higher than a recent study conducted in Nigeria (3.0%), and lower than studies from other African countries [23-25] among HIVHBV coinfected patients. We observed more severe fibrosis in HIV/HBV and HBV-mono infected patients aged 38-47 years, this agreed with earlier study that clarified that sever fibrosis increases with age [25].

In the sex factor, the distribution showed female predominance amongst those, with more severe liver fibrosis, and no statistically significant association, p-0.58 (Table 2). This was in agreement with earlier findings that sex was not associated with higher risk for fibrosis, [23] but does not corroborate that male sex have higher risk of fibrosis than female. We also observed no significant difference between the groups as regards to serum ALT, AST, Haemoglobin, WBC, Lymphocytes, Neutrophil, Creatinine, Albumin and Bilirubin, but found statistically significant association with Platelet count, which was lower in HBV-mono infected patients. However, serum albumin was lower among HBV-mono infected patients, whereas total bilirubin was lower in HIV/HBV coinfected patients, though these parameters were not analyzed in relation to liver fibrosis (Table1). This finding was not in agreement with earlier study that showed positive correlation of serum enzymes, [26] but corroborate with earlier study, [23] which does not show any significant association with serum enzymes. Also observed, was alcohol intake, there was no significant difference between the HIV/HBV and HBV-mono infected patients, more patients had <5kpa. We did not measure the quantity of alcohol intake, nor establish the impact of alcohol and liver fibrosis since the patients were not followed up. However, chronic and high alcohol consumption may lead to cirrhosis and is associated with higher risk of liver disease progression to cirrhosis [27].

In this study, although HBV viral load showed no statistical significance but more HIV/HBV coinfected patients had lowest levels of HBV viral load compared to HBV-mono infected patients, which had higher levels (20-20000 cps/mL) suggesting that the coinfected patients usually start tenofovir combination earlier compared to HIV-mono infected patients. This also means that the HIV-mono infected patients should be encouraged to initiate tenofovir monotherapy earlier at designated treatment hospitals. Though there was no significant association with severe liver fibrosis, but we found higher HBV-DNA levels in HBV-mono infected patients with severe liver

fibrosis than in those with mild-moderate liver fibrosis score. This was contrary to earlier report that severe liver fibrosis was strongly correlated with higher viral load [28]. However, recent findings in Ghana showed that HBV DNA load was strongly associated with TE measurements, [22] including another study in ART-naïve HIV/HBV-coinfected subjects in Nigeria [21]. Similarly, a study in HBV-infected patients from Taiwan, reported HBV DNA load was the strongest predictor of liver disease progression to cirrhosis over time [29]. Our results support the evidence of the benefits of tenofovir combination therapy on virological and clinical outcomes in chronic hepatitis B patients on ART.

In both HIV/HBV and HBV-mono infected patients, the prevalence of Thrombocytopenia and liver fibrosis was more among HBV-mono, with no statistical significance association, but had a statistical association with HIV/HBV coinfected patients. It's interesting to note, that thrombocytopenia is a common haematological disorder in patients with chronic liver disease, and the cause is multifactorial [30]. However, in some African populations, the association of TE score and platelet count can be influenced by many factors, and thrombocytopaenia, a common disorder may be influenced by inflammatory conditions and perhaps infections due to malaria, endemic parasites or drugs induced [31]. Therefore, other possible causes include suppression of platelet production in the bone marrow, splenic sequestration of platelets, and decreased haematopoietic growth factor thrombopoietin activity [30]. Although mild to moderate thrombocytopaenia is common among chronic hepatitis patients but usually does not interfere with management, but may require therapeutic approach to replace deficient factors to avoid complications [31]. Although the impact of this association was not established, but studies have shown that decreased thrombopoietin (TPO) production play an important role in advanced liver disease patients and thrombocytopaenia. The significant difference among the HIV/HBV may be due to HIV-induced thrombocytopaenia, hepatitis or other drugs related factors, though the suggestion could unlikely in the group as majority of the patients had normal platelets with high median value of 259 109/L with normal ranges of AST and ALT values (Table1).

This study had some limitations such as inability to measure HBeAg as a surrogate marker for active HBV viral replication. The other limitations include; lack of data on smoking, alcohol consumption measurement including locally brewed alcohol (Burukutu) which are sources of aflatoxin and hepatotoxicity due to herbal formulations. Also, the diagnostic inaccuracy of TE that measures the shear wave speed through the liver indicating stiffness, but not exact amount of fibrosis, and waist circumference interference due to overweight [32].

CONCLUSION

In this study, sex and thrombocytopenia were significantly associated with severe liver fibrosis among HIV/HBV coinfected patients. Tenofovir regimen is a predictor of these good outcomes in HIV/HBV-coinfected HBV-mono infected patients. With the observed substantial proportion (13.0%) of severe liver fibrosis among HIV/HBV-coinfected and HBV-mon infected patients supports the need for continuous routine HBV screening in the HIV clinics, and prioritized tenofovir use in the treatment of chronic hepatitis B patients. Therefore, further studies are needed to monitor chronic hepatitis B patients using TE and investigate the effect of long-term antiviral therapy on the liver.

AUTHOR'S CONTRIBUTIONS STATEMENT

JA Conceptualized and designed the research plan and prepared the manuscript. MPD performed background literature and review manuscript, JB, CSR, FBY and GAAC organized and participated in the main role of recruitment process. CO FBY carried out part of the laboratory tests, OJO conducted the data analysis, and OA participated in the manuscript draft and revision, PA collected and supervised all clinical issues of patients. OA, ASS and EO revised and approved the article.

CONFLICTS of INTEREST

All authors declared no conflict of interests.

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