

Seroprevalence and Risk Factors of Hepatitis B virus Infection among People Living with HIV on Antiretroviral Treatment in Three Regions of Cameroon

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Abstract

Although the prevalence of Hepatitis B Virus (HBV) in people living with HIV (PLHIV) is high globally, it remains variable in different settings. Few studies have been conducted on Hepatitis B in PLHIV on antiretroviral treatment in Cameroon. This study sought to determine the seroprevalence and risk factors of HBV among PLHIV on antiretroviral treatment (ART) from three regions of Cameroon. This hospital-based cross-sectional study was conducted from June 2016 to April 2017 among PLHIV on ART in the Littoral, Northwest and Southwest regions of Cameroon. Participants' information was obtained using a questionnaire and a review of medical records. HBV seromarkers were diagnosed using immunochromatographic methods. Data was analysed using descriptive statistics and logistic regression models at a 95% CI and 5% significance level. HBV/HIV coinfection prevalence was 8.7% among 952 participants in the three regions, 9.4% in the Littoral, 7.5% in the Northwest, and 8.5% in the Southwest regions. Males had higher odds of coinfection (OR: 3.63, 95%CI: 0.080-16.50 $p=0.09$). Participants with secondary education were less likely to be HBsAg positive (OR=0.17, 95%CI: 0.02-0.93; $p=0.042$). Those with a history of tattooing had about four times more chances of coinfection (AOR: 3.4, 95% CI: 0.79-12.39, $p=0.097$). Among co-infected participants, HBsAb positivity was significantly associated with age ($p=0.030$), and HBeAg positivity with ALT ($p=0.043$) and AST levels ($p=0.039$). HBV/HIV coinfection was high among study participants. There is a need to routinely screen for HBV and its different seromarkers in PLHIV on antiretroviral treatment to improve the management of patients with coinfection and reduce complications and death from liver disease in PLHIV.

Keywords: Cameroon, Coinfection, Hepatitis B Virus, People Living with HIV, Prevalence.

Introduction

Infection with the Hepatitis B virus is a significant cause of chronic hepatitis, liver cirrhosis, and hepatocellular carcinoma. About 10% of people with human immunodeficiency virus (HIV) are also infected with HBV, owing to their common transmission routes [1]. About 90% of HIV-infected persons have been positive for at least one HBV serologic marker;

coinfection with chronic hepatitis is between 5%-40%. Mortality from liver disease is about 17 times higher in co-infected individuals than in those with HBV mono-infection [2]. In PLHIV, liver disease is a predominant cause of non-AIDS mortality, with about 13%–18% of all deaths attributed to a liver-related disease or condition [3]. HIV can infect different cells in the liver, causing enhanced intrahepatic

apoptosis, activation, and fibrosis. HIV modifies the permeability of the gastrointestinal tract, causing increased volumes of lipopolysaccharide (LPS) circulating. Circulating polysaccharides can impair liver function by stimulating Kupffer cells (KCs) and human Stellate cells (HSCs) to produce proinflammatory cytokines and chemokines whose presence brings about activated lymphocytes and monocytes to the liver, increasing fibrosis [4]. Factors that influence the progression of liver disease in HIV/HBV coinfection include HBV, Intrahepatic HIV, gut, immune system, and clinical and HSC activation [5]. HIV induces immune suppression due to a decline in CD4⁺ T-cell counts, Immune activation, apoptosis in lymphocytes and hepatocytes, oxidative stress, inflammation, impaired immune responses, promotion of retroviral infection of HSC and Kupffer cells, and microbial translocation [6]. HBV may affect immunological and virological responses to ART in HIV-infected persons and increase the risk of hepatotoxicity [7].

With better access to effective antiviral therapy active against HIV and HBV and simplified treatment algorithms, treating co-infected patients has become more accessible [8]. However, it is still challenging in developing countries where access to HBV testing is not routine. According to WHO guidelines, PLHIV should be tested for HBsAg, HBcAbs, and anti-HBs. Those who are HBsAg positive should do quantitative HBV DNA and be screened for hepatitis delta antibodies [9]. Evidence shows that people with HIV/HBV coinfection should be placed on HIV antiviral therapy following diagnosis, irrespective of the clinical HIV stage or the CD4 count [10]. ART regimens in HBV/HIV patients should aim at high viral suppression rates of both HIV and Hepatitis B [11]. They should contain two agents with potent activity against HBV: four HIV antiretroviral medications are indicated. Reverse transcriptase inhibitors have activity against both viruses: Tenofovir, emtricitabine,

and lamivudine [12]. Tenofovir-containing regimens are highly active against HBV. They also have a high genetic barrier for developing HBV drug resistance and are active against variants resistant to lamivudine- or emtricitabine [11].

Different studies conducted in Cameroon have shown different HBV/HIV coinfection prevalence. Bigna et al. 2018 reported a seroprevalence of hepatitis B in HIV-infected persons at 11.2% in Cameroon [13]. Other studies from Cameroon reported an HBV/HIV coinfection prevalence of 8.3% among adults starting antiretroviral treatment in 2010 [14]. In 2011, the Northwest Region reported a coinfection prevalence of 12.6%, while the Littoral Region reported a prevalence of 6.4% in 2014. in 2014 [16]. Increased access to treatment has contributed to higher life expectancy in PLHIV globally [17]. These gains are, however, threatened by the rising trends in liver disease-related deaths in PLHIV, with liver disease from hepatitis among the leading causes [18,19]. Although a few studies estimated the prevalence of HBV/HIV coinfection using HBsAg as a marker of HBV positivity [20-23], none had attempted to establish the serological profile of HBV/HIV co-infected persons. This study sought to add to existing knowledge on the prevalence of HBV in PLHIV on antiretroviral treatment, the distribution of HBV sero-markers in HIV/HBV coinfection and what factors favour coinfection in three regions of Cameroon.

Materials and Methods

Study Design

The study used a multicenter hospital-based cross-sectional design, conducted from June 2016 to April 2017 among people living with HIV/AIDS on antiretroviral treatment, attending the HIV care and treatment centres of 04 health facilities in three regions of Cameroon.

Setting

The study was conducted in three regions of Cameroon: The Littoral, Northwest, and Southwest Regions. Study participants were recruited between June 2016 and April 2017 from Nylon District Hospital and Laquintinie Hospital in the littoral Region. In the Northwest and Southwest regions, from the Bamenda Regional Hospital and the Buea Regional Hospital HIV Care and Treatment Centres, respectively. All selected sites were in the regional headquarters and had similar sociodemographic characteristics.

Study Population

The study population consisted of PLHIV on ART visiting the selected health facilities for routine follow-up, CD4+ T lymphocyte counts assessment, viral loads sample collection and results return, enhanced adherence counselling, and antiretroviral drug pick-up. Participants were recruited for the study through consecutive sampling. Participants were above 15 years old, and only those who provided signed informed consent or assent forms were enrolled in the study.

Sample Size

The study included multiple sites, and the formula below was used to calculate the minimum sample sizes for each health facility. The minimum sample size for the study was obtained by summing up the sample sizes for each health facility.

$$n' = \frac{n}{1 + \frac{z^2 \times \rho(1 - \rho)}{\varepsilon^2 N}}$$

z is the z score, ε is the margin of error, N is the population size and, in this case, the number of PLHIV enrolled in the respective health facilities, HIV care, and treatment centres. ρ Is the population proportion for the area. We used N as 4000 for the Northwest and a population proportion of HBV/HIV coinfection of 12.6% [15]; N as 3500 with 6.1% coinfection prevalence in the southwest [24], and N as 7000

and 6000 for Laquintinie and Nylon district hospitals, with a prevalence of 6.4% in the Littoral [16]. A total of 952 PLHIV participated in the study.

Laboratory Analysis

Whole blood was collected into 5ml pre-labelled dry tubes for each participant. The tubes were allowed to stand for 15 to 30 minutes after collection, then centrifuged at 3000 rpm for 5 minutes, and the serum was collected for HBV sero-markers analysis and liver biochemistry test. The *DiaSpot* Hepatitis B Surface Antigen test strip (Hangzhou, China), a rapid one-step chromatographic immunoassay, was used to detect HBsAg qualitatively. Only reactive samples for hepatitis B surface antigen with *DiaSpot* Hangzhou, China, were analysed for other HBV sero-markers. Using a 05 parameters rapid screening test for Hepatitis B biomarkers by CTK BIOTECH, San Diego, USA, HBsAg positivity was confirmed and the presence of 04 other HBV confirmation of HBsAg positivity and detection of other HBV seromarkers; Hepatitis B surface antibody (HBsAb), Hepatitis B envelope antigen (HBeAg), Hepatitis B envelope antibody (HBeAb), and hepatitis B core antibody (HBcAb). Participants who were HBsAg positive were considered Hepatitis B positive. Participants were grouped as HIV only or HBV/HIV co-infected.

Data Collection and Statistical Analysis

Questionnaires were administered to collect information on sociodemographic characteristics and medical history. Sociodemographic data such as age, Sex, employment status, marital status, and HBV exposure history were obtained using a pre-tested questionnaire. Data on participant medical history, such as HIV ART regimen, duration of treatments, other health conditions, treatment adherence, and most recent HIV viral load results, were obtained from a review of medical records (Patient files) using an

information extraction form. All data collected was entered into an Excel file for later analysis. To reduce bias, all staff members who facilitated the study were trained. Questionnaires were pre-tested. The questionnaire was read out to clients who had low literacy levels.

Data obtained were keyed into a computer using Microsoft Excel 2016 (Microsoft Corporation, Inc., USA), cleaned, and analysed using the Statistical Package for Social Sciences (SPSS) version 25.0. Descriptive statistics were used to summarise the data, and the association between sociodemographic variables and risk factors with HBV/HIV coinfection was determined using Fisher or chi-square statistics and the logistic regression models.

P-values <5% were considered statistically significant.

Ethical Approval

Ethical approval was obtained from the Institutional Review Board of the Faculty of Health Sciences of the University of Buea (Reference No: 2016/439/UB/FHS/IRB). The administrative authorisation was obtained from the Regional Delegation of the Ministry of Public Health in each Region and the health facility administration. A signed written consent or permission form was obtained from

each participant after the purpose of the study was explained to them. The consent form was read and signed voluntarily.

Results

Characteristics of Study Participants

Table 1 shows that 952 PLHIV were enrolled in the study. The majority, 731(76.8%), were females compared to 221 (23.4%) for males. Self-employment in the informal sector was common (58.8%). About half of the participants consumed some form of alcohol (51.2%). A blood transfusion history and a history of tattooing were reported in 16.5% and 28.5% of participants, respectively. The mean CD4+T-lymphocytes count $\pm$ SD in the study was 448 ± 260 cells/mm³.

HBV Seroprevalence in PLHIV on ART in the Study

Of the 952 study participants enrolled from all three regions between June 2016 and April 2017, 83 were positive for HBsAg, making an HBV/HIV coinfection prevalence of 8.7 (8.7%: 95% CI: 7.1–10.7%) (Figure 1).

The mean age ($\pm$ SD) was 41.3($\pm$ 10.4) years, with most participants in the age groups 31 to 40 years 316(33.2%) and 41 to 50 years 317(33.3). Most participants were married 408, 41.3% and had at least a secondary school level of education.

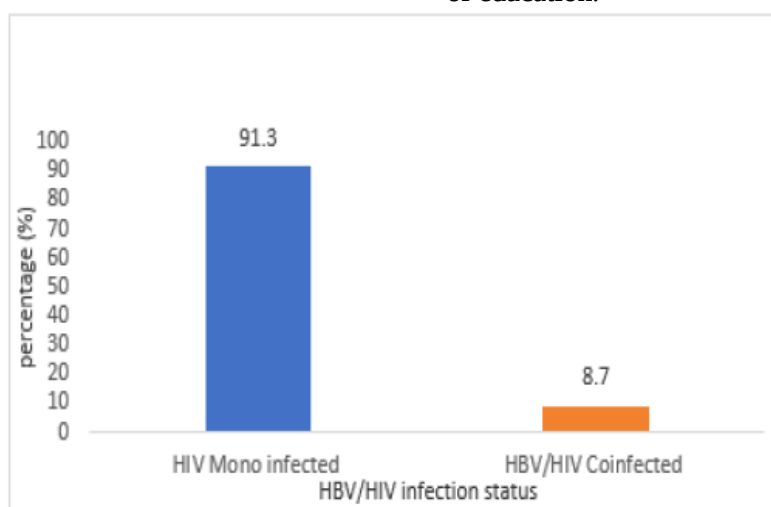


Figure 1. Prevalence of HBV among PLHIV on ART in the Littoral, Northwest, and Southwest regions of Cameroon, 2016- 2017

Table 1. Characteristics of PLHIV on ART from the littoral, Northwest and Southwest regions of Cameroon
2016- 2017

Characteristic		Frequency (N=952)	Percentage (%)
Sex	Female	731	76.8
	Male	221	23.2
Age group	<31 years	109	11.5
	31-40 years	316	33.2
	41-50 years	317	33.3
	51-60 years	171	18
	>60 years	39	4.1
Marital status	Divorced	36	3.8
	Married	408	41.3
	Single	360	37.8
	Widowed	148	15.5
Educational level	Informal	31	3.3
	Primary	368	38.7
	Secondary	480	50.4
	Tertiary	73	7.7
Occupation	Employed	168	17.6
	Retired	6	0.6
	Self-employed	560	58.8
	Unemployed	218	21.3
Smoking	No	900	94.5
	Yes	52	5.5
Alcohol consumption	No	456	47.9
	Yes	496	51.2.1
blood transfusion	No	795	83.5
	Yes	157	16.5
History of Tattooing	No	289	71.5
	Yes	115	28.5
	<200 cells/ μ l	97	14.8
	200-350 cells/ μ l	150	21.3
	>350 cells/ μ l	408	61.2
Duration of ART treatment	< 1 year	49	5.2
	1-4 years	362	38.0
	5-9 years	326	34.2
	$\geq$ 10 years	215	22..6
Region of residence	Littoral	524	55.0
	Northwest	200	21.0
	Southwest	228	23.9

HBV Seroprevalence in PLHIV on ART by Region

The prevalence by region was 9.4 % in the Littoral region, 7.5% in the Northwest, and 8.5% in the Southwest (Figure 2).

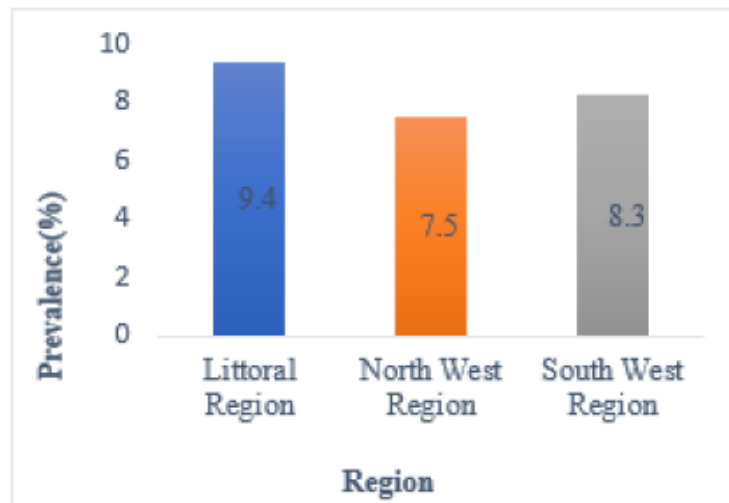


Figure 2. HBV/HIV coinfection prevalence in PLHIV on ART by region; Littoral Northwest and Southwest regions of Cameroon.

Prevalence of HBV Sero-markers in HBV/HIV Co-infected Study Participants

Among the 83 HBV/HIV co-infected participants from all three regions (Littoral, Northwest and Southwest), 8 participants (9.6%) were positive for HBsAb (95% CI: 3.3–15.9%). This implies that 08 participants had

HBsAg/HBsAb simultaneously, as all 83 study participants were HBsAg positive, 6 participants (7.2%) were positive for HBeAg (95% CI: 1.6–11.2.8%), 33 participants (39.8%) were positive for HBeAb (95% CI: 29.3–50.3%), and 41 participants (49.4%) were positive for HBcAb (95% CI: 38.6–60.2%) (Figure 3).

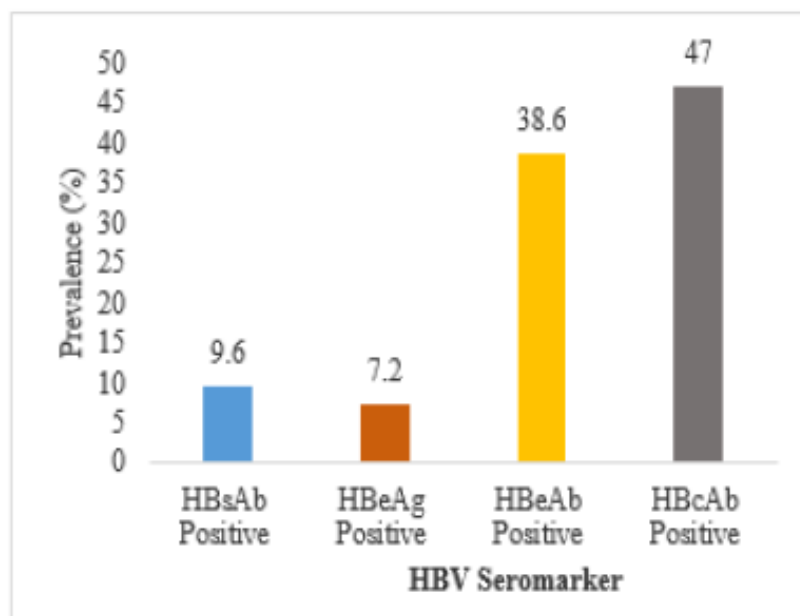


Figure 3. Prevalence of HBsAb, HBeAb, HBeAg, and HBcAb among HBV/HIV co-infected participants in the Littoral Northwest and Southwest Regions of Cameroon, 2016-2017

Factors Associated with HBV Coinfection in PLHIV on ART

The prevalence of HBV/HIV coinfection in females was 6.7% compared to 15.4% in males. Males were about four times more likely to have HBV than females. This difference was, however, found to be insignificant after adjusting for confounding variables (AOR: 3.63, 95% CI: 0.80-16.50, $p=0.095$). Older participants were more likely to be co-infected than those below 31, although the association was insignificant. Participants with at least a secondary school level of education had lower odds for HBV/HIV

coinfection when compared to those with had not received education and those who went ended their education at primary school (AOR:0.13, 95% CI: 0.02-0.93, $p = 0.042$). Participants with a history of tattooing had about three times more chances of HBV/HIV coinfection (AOR: 3.4, 95% CI: 0.79-12.39, $p = 0.097$; Table 2). Regarding the duration of antiretroviral treatment (ART), although the association was not significant, participants who were less than one year on ART were more likely to be co-infected than those who had been longer on ART (AOR:1.67, 95% CI: 0.08-34.16, $p = 0.739$).

Table 2. Logistic regression of factors associated with HBV/HIV coinfection in PLHIV on ART in the Littoral, Northwest and Southwest regions of Cameroon

Variable		HIV -only n(%)	HBV/HI V n(%)	Crude OR	95% CI	p- value	Adjusted OR	95% CI	p-value
Sex	Female	682(93.3)	49(6.7)	1.00	-	-	1.00	-	-
	Male	187(84.6)	34(15.4)	2.53	1.59-4.04	<0.001	3.63	0.80-16.50	0.095
	Total	869(91.3)	83(8.7)						
Age group	<31 years	96(88.1)	13(11.9)	1.00	-	-	1.00	-	-
	31-40 years	292(92.4)	24(7.6)	0.61	0.30-1.24	0.170	0.80	0.06-10.69	0.864
	41-50 years	287(90.5)	30(9.5)	0.77	0.39-1.54	0.463	2.85	0.28-28.55	0.373
	51-60 years	159(93.0)	12(7.0)	0.56	0.24-1.27	0.165	2.74	0.24-31.03	0.416
	>60 years	35(89.7)	4(10.3)	0.84	0.26-2.76	0.779	5.15	0.14-185.45	0.370
	Total	869(91.3)	83(8.7)						
Marital status	Single	326(90.6)	34(9.4)	1.00	-	-	1.00	-	-
	Married	377(92.4)	31(7.6)	0.79	0.47-1.31	0.360	0.20	0.04-1.03	0.054
	Divorced	30(83.3)	6(16.7)	1.92	0.75-4.93	0.177	-	-	-
	Widowed	136(91.9)	12(8.1)	0.85	0.43-1.68	0.634	0.53	0.09-3.06	0.481
	Total	869(91.3)	83(8.7)						
Educational level	Informal	25(80.6)	6(19.4)	1.51	0.50-4.60	0.467	0.99	0.04-22.38	0.996
	Primary	339(92.1)	29(7.9)	0.54	0.25-1.16	0.114	0.52	0.08-3.43	0.496
	Secondary	442(92.1)	38(7.9)	0.54	0.26-1.14	0.107	0.13	0.02-0.93	0.042
	Tertiary	63(86.3)	10(13.7)	1.00	-	-	1.00	-	-
	Total	869(91.3)	83(8.7)						
Occupation	Employed	153(91.1)	15(8.9)	1.00	-	-	1.00	-	-
	Retired	6(100.0)	0(0.0)	-	-	-	-	-	-
	Self-employed	510(91.1)	50(8.9)	1.00	0.55-1.83	1.000	2.44	0.42-14.16	0.319

	Unemployed	200(91.7)	18(8.3)	0.92	0.45-1.88	0.815	2.59	0.40-16.72	0.318
	Total	869(91.3)	83(8.7)						
Smoking	No	823(91.4)	77(8.6)	1.00	-	-	1.00	-	-
	Yes	46(88.5)	6(11.5)	1.39	0.58-3.37	0.460	1.45	0.05-38.17	0.824
	Total	869(91.3)	83(8.7)						
Alcohol consumption	No	409(89.7)	47(10.3)	1.00	-	-	1.00	-	-
	Yes	460(92.7)	36(7.3)	0.68	0.43-1.07	0.097	0.27	0.07-1.09	0.066
	Total	869(91.3)	83(8.7)						
History of blood transfusions	No	724(91.1)	71(8.9)	1.00	-	-	1.00	-	-
	Yes	145(92.4)	12(7.6)	0.84	0.45-1.60	0.602	0.12	0.01-1.48	0.099
	Total	869(91.3)	83(8.7)						
History of Tattooing	No	263(91.0)	26(9.0)	1.00	-	-	1.00	-	-
	Yes	102(88.7)	13(11.3)	1.29	0.64-2.61	0.479	3.14	0.79-12.39	0.097
	Total	869(91.3)	83(8.7)						
CD4+ T cell count	<200 cells/μl	86(88.7)	11(11.3)	1.74	0.83-362	0.142	0.90	0.13-6.41	0.913
	200-350 cells/μl	132(88.0)	18(12.0)	1.85	0.99-3.46	0.053	1.60	0.38-6.70	0.518
	>350 cells/μl	380(93.1)	28(6.9)	1.00	-	-	1.00	-	-
	Total	869(91.3)	83(8.7)						
Duration of ART treatment	< 1 year	41(83.7)	8(16.3)	2.14	0.87-5.24	0.300	1.67	0.08-34.16	0.739
	1-4 years	331(91.4)	31(8.6)	1.03	0.56-1.88	0.936	0.60	0.11-3.45	0.570
	5-9 years	300(92.0)	26(8.0)	0.95	0.51-1.78	0.869	0.49	0.11-2.20	0.352
	≥ 10 years	197(91.6)	18(8.4)	1.00	-	-	1.00	-	-
	Total	869(91.3)	83(8.7)						
Region of Residence	Littoral	475(90.6)	49(9.4)	1.14	0.65-1.98	0.655	-	-	-
	Northwest	185(92.5)	15(7.5)	0.89	0.44-1.81	0.751	-	-	-
	Southwest	209(91.7)	19(8.3)	1.00	-	-	1.00	-	-
	Total	869(91.3)	83(8.7)						

Factors Associated with HBV Sero-markers in HBV/HIV Co-infected Participants on ART

As shown in Table 3, the study found no association between HBV sero-markers in HBV/HIV co-infected participants and factors like Sex, employment status, marital status, Alcohol consumption, a history of tattooing, blood transfusion, and CD4+ T cells count at 95% CI. There was a significant association

between Age and HBsAb positivity, with fewer participants in the age group above 60 having HBsAbs ($P=0.030$). HBeAb positivity and HBcAb positivity were related to the Region of the study, $P<0.001$ for both sero-markers. The study also found that Liver enzymes ALT and AST were associated with HBeAg and HBcAb positivity among study participants, $P=0.043$ and $P=0.039$, respectively, for ALT and $P=0.001$ and $P=0.018$ for AST.

Table 3. Factors associated with HBV sero-markers in HBV/HIV co-infected persons on ART in the Littoral, Northwest and Southwest regions of Cameroon 2016-2017

Variables		Total	HBsAb Positive n (%)	HBeAg Positive n (%)	HBeAb Positive n (%)	HBcAb Positive n (%)
Total	Co-infected	83(100%)	08 (9.6)	06 (7.2)	32(38.6)	39 (47.0)
			$\chi^2 = 4.108$, p-value = 0.061	$\chi^2 = 0.199$, p-value = 0.701	$\chi^2 = 0.040$, p-value = 0.842	$\chi^2 = 3.878$, p-value = 0.071
Sex	Male	34 (41.0)	06 (17.6)	02 (5.9)	13 (38.2)	12 (35.3)
	Female	48 (59.0)	02 (4.2)	04 (8.5)	19 (40.4)	27 (57.4)
			$\chi^2 = 3.907$, p-value = 0.372	$\chi^2 = 2.796$, p-value = 0.570	$\chi^2 = 5.053$, p-value = 0.270	$\chi^2 = 3.062$, p-value = 0.559
Age	<31 years	13 (15.7)	1 (7.7)	02 (16.7)	08 (66.7)	08 (66.7)
	31-40 years	24 (28.9)	04 (17.7)	01 (4.3)	09 (39.1)	12 (52.2)
	41-50 years	30 (36.1)	01 (3.3)	03 (10.0)	09 (30.0)	13 (43.3)
	51-60 years	12 (14.5)	02 (16.7)	0 (0.0)	05 (41.7)	05 (41.7)
	>60 years	04 (4.8)	0 (0.0)	00 (0.0)	01 (25.0)	01 (25.0)
			$\chi^2 = 8.941$, p-value = 0.030	$\chi^2 = 2.158$, p-value = 0.54	$\chi^2 = 5.053$, p-value = 0.272	$\chi^2 = 3.208$, p-value = 0.544
Academic Qualification	Informal	06 (7.2)	0 (0.0)	0 (0.0)	2 (33.3)	3 (50.0)
	Primary	29 (34.9)	2 (6.9)	1 (3.4)	9 (31.0)	10 (34.5)
	Secondary	38 (45.8)	3 (8.1)	5 (13.9)	16 (44.4)	20 (55.6)
	Tertiary	10 (12.0)	3 (30.0)	0 (0.0)	5 (50.0)	6 (60.0)
			$\chi^2 = 4.200$, p-value = 0.183	$\chi^2 = 2.656$, p-value = 0.370	$\chi^2 = 1.879$, p-value = 0.638	$\chi^2 = 3.591$, p-value = 0.315
Marital Status	Single	52 (62.7)	5 (9.8)	3 (6.0)	22 (44.0)	26 (52.0)
	Married	31 (37.3)	3 (9.7)	3 (9.7)	10 (32.3)	13 (41.9)
			$\chi^2 = 0.00$, p-value = 0.650	$\chi^2 = 0.377$, p-value = 0.419	$\chi^2 = 1.104$, p-value = 0.208	$\chi^2 = 0.776$, p-value = 0.257
Employment Status	Employed	15 (18.1)	3 (20.0)	1 (6.7)	7 (46.7)	7 (46.7)
	Self-Employed	50 (60.2)	3 (6.1)	2 (4.2)	18 (37.5)	21 (43.8)
	Unemployed	18 (21.7)	2 (11.1)	3 (16.7)	7 (38.9)	11 (61.1)
			$\chi^2 = 2.750$, p-value = 0.185	$\chi^2 = 2.923$, p-value = 0.187	$\chi^2 = 0.484$, p-value = 0.776	$\chi^2 = 1.605$, p-value = 0.502
Smoking	Yes	06 (7.2)	07 (9.2)	06 (7.9)	31 (40.8)	37 (48.7)
	No	77 (92.8)	01 (16.7)	0 (0.0)	01 (20.0)	2 (40.0)
			$\chi^2 = 0.351$, p-value = 0.471	$\chi^2 = 0.426$, p-value = 0.674	$\chi^2 = 0.848$, p-value = 0.339	$\chi^2 = 0.142$, p-value = 0.536

Variables		Total	HBsAb Positive n (%)	HBeAg Positive n (%)	HBeAb Positive n (%)	HBcAb Positive n (%)
Alcohol Consumption	Yes	36 (43.4)	2 (4.3)	4 (8.5)	17 (36.2)	22 (46.6)
	No	47 (56.6)	6 (17.1)	2 (5.9)	15 (44.1)	17 (50)
			$\chi^2 = 3.784$, p-value = 0.590	$\chi^2 = 0.199$, p-value = 0.502	$\chi^2 = 0.521$, p-value = 0.311	$\chi^2 = 0.080$, p-value = 0.477
Blood Transfusion	Yes	12 (14.5)	08 (11.4)	05 (7.1)	29 (41.4)	34 (48.6)
	No	71 (85.5)	0 (0.0)	01 (9.1)	03 (27.3)	05 (45.5)
			$\chi^2 = 1.520$, p-value = 0.265	$\chi^2 = 0.053$, p-value = 0.596	$\chi^2 = 0.797$, p-value = 0.293	$\chi^2 = 0.037$, p-value = 0.553
History of Tattooing	Yes	13 (15.7)	06 (23.1)	0 (0.0)	12 (46.2)	18 (69.2)
	No	26 (31.3)	01 (7.7)	02 (16.7)	08 (66.7)	10 (83.3)
			$\chi^2 = 1.393$, p-value = 0.237	$\chi^2 = 4.574$, p-value = 0.094	$\chi^2 = 1.386$, p-value = 0.205	$\chi^2 = 0.842$, p-value = 0.309
CD4+ T cell Count	<200 cells/ μ l	12 (14.5)	01 (8.3)	0 (0.0)	01 (8.3)	01 (8.3)
	200-350 cells/ μ l	17 (20.5)	02 (12.5)	01 (6.3)	07 (43.8)	0.8 (50.0)
	>350 cells/ μ l	28 (33.7)	0 (0.0)	03 (10.7)	10 (35.7)	12 (42.9)
			$\chi^2 = 3.639$, p-value = 0.118	$\chi^2 = 1.080$, p-value = 0.802	$\chi^2 = 4.344$, p-value = 0.120	$\chi^2 = 5.978$, p-value = 0.064
Line of ART	First Line	74 (89.2)	07 (9.6)	05 (6.9)	28 (38.9)	33 (45.8)
	Second Line	09 (10.8)	01 (11.1)	01 (11.1)	04 (44.4)	06 (66.7)
			$\chi^2 = 0.021$, p-value = 0.623	$\chi^2 = 0.203$, p-value = 0.519	$\chi^2 = 0.103$, p-value = 0.508	$\chi^2 = 1.127$, p-value = 0.369
Knowledge of HBV Status	Yes	12 (14.5)	07 (10.0)	6 (8.7)	26 (37.7)	33 (47.8)
	No	71 (85.5)	01 (8.3)	0 (0.0)	06 (50.0)	06 (50.0)
			$\chi^2 = 0.032$, p-value = 0.668	$\chi^2 = 1.127$, p-value = 0.369	$\chi^2 = 0.649$, p-value = 0.310	$\chi^2 = 0.019$, p-value = 0.568
ALT	Normal	50 (60.2)	04 (12.1)	0 (0.0)	07 (21.9)	8 (25.0)
	High	33 (39.8)	04 (8.2)	06 (12.2)	25 (51.0)	31 (63.3)
			$\chi^2 = 0.351$, p-value = 0.409	$\chi^2 = 4.232$, p-value = 0.043	$\chi^2 = 0.021$, p-value = 0.623	$\chi^2 = 11.353$, p-value = 0.001
AST	Normal	34 (41.0)	04 (8.2)	01 (2.1)	18 (37.5)	18 (37.5)
	High	49 (59.0)	04 (12.1)	5 (15.2)	14 (42.4)	21 (63.6)
			$\chi^2 = 0.351$, p-value = 0.409	$\chi^2 = 4.869$, p-value < 0.039	$\chi^2 = 0.198$, p-value = 0.414	$\chi^2 = 5.351$, p-value = 0.018

Discussion

An HBV/HIV coinfection prevalence of 8.7% was obtained from the 952 participants enrolled in the study. This result supports previous findings from Mathews et al. (2014) in a data review of HIV/ Hepatitis coinfection in people living with HIV, which estimates prevalence between 6 and 25% in sub-Saharan Africa [25]. In other studies in Cameroon, a prevalence of 8.9% was reported by Molu et al. in HIV-infected patients starting treatment in Mfou, a rural health district setting [26]. On the other hand, Bigna et al. reported a higher HBV prevalence of 12.9% in HIV-infected persons from 7 out of 10 regions of Cameroon [13]. Differences in sample size selection may explain the difference in results. Prevalence of 9.4%, 7.5%, and 8.5% were recorded in the Littoral, Northwest, and Southwest regions, respectively. Although the difference in prevalence was insignificant, it was higher in the Littoral Region with greater odds for coinfection (OR: 1.14, 95% CI: 0.65-1.98). This result is likely because Littoral is the socioeconomic capital of Cameroon, a melting point of different socioeconomic classes, with risk behaviour that may favour horizontal transmission of STIs, including HBV. HBV and HIV have shared routes of transmission and some common risk factors, and this can explain the high coinfection prevalence in the different studies [27].

In this study, there was no significant association between Sex and HBV/HIV coinfection. However, males were more likely to be co-infected than females, 15.4% and 6.7% respectively. This result is comparable to that of a study of PLHIV in Nigeria, where Diwe et al. also found no association between Sex and HBV/HIV coinfection [28]. On the other hand, Akindigh et al. (2019) found that there is a strong association between male Sex and HBV/HIV coinfection in another study in Nigeria [29]. In Cameroon, Assob et al. also observed no significant association between Sex and HBV infection in PLHIV [16], while Luma et al. (2016) found evidence of an association between

Sex, opportunistic infections and multiple sexual partners with coinfection [24]. Differences in findings may be due to the epidemiologic settings and sample sizes.

Though no significant association was observed between CD4+T-Lymphocyte count and HBV coinfection in this study, HBV/HIV coinfection prevalence was higher in participants with lower CD4+ T-Lymphocyte counts, less than 200 cells/mm³ (11.3%) and 200 to 350 cells/mm³ (12%), respectively. Moreover, those with CD4+T-Lymphocyte counts between 200-350 cells/mm³ were more likely to be co-infected. Rana et al. argued that people with HIV/HBV coinfection have lower CD4 T cell counts and higher mortality [30]. Molu et al. also found that coinfection with HBV was higher in patients with low CD4+ count in Cameroon; however, this difference was insignificant [26]. Although reasons for this association may vary, Sarmati and Malagnino have argued that coinfection affects the “viral-immunological status” of people with coinfection, which can lead to decreased CD4+T-lymphocytes and recovery. They also associate low CD4 count with an increased risk of liver fibrosis and increasing mortality in co-infected persons [31].

Higher coinfection rates were observed for PLHIV who had been on antiretroviral treatment for less than one year (14.3%) compared to those with more prolonged treatment. However, the relationship between the duration of treatment and HBV/HIV coinfection was not significant. The presence of HBsAg in participants with different durations of treatment suggests new HBV infection in HIV-infected patients on ART. A study in Uganda found a high prevalence of HBV in PLHIV naive or on ART [32]. Findings from this study reinforce the need to screen for Hepatitis B markers routinely in HIV-infected persons and follow national guidelines on managing HBV/HIV coinfection to reduce morbidity and mortality.

The prevalence of HBsAb was 9.6% among the 83 HBV/HIV co-infected participants. PLHIV have been observed to have lower

HBsAb rates. There is a need to scale up efforts to increase HBsAb-positive rates among HIV patients to prevent horizontal transmission [33]. Previously, HBsAg/HBsAb coexistence was uncommon. However, occurrence has increased with vaccine promotion and the use of different antiretroviral, as well as improvements in medical diagnostic techniques. Other factors that may favour this coexistence include Host immune status, the mutation in the viral genome, or host genetic factors [34]. HBeAg and HBeAb prevalence were 7.2% and 39.8% in HBV/HIV co-infected participants. In a similar study in Brazil, of 21 HIV-positive participants, 7 (33.3%) had HBeAg, and 9 (42.9%) had anti-HBe. [35]. HIV coinfection substantially decreases the rate of hepatitis B e antigen (HBeAg) clearance by up to fivefold. It increases the risk of HBV DNA replication and reverses the conversion from HBsAb status to HBsAg. [2]. The prevalence of HBcAb was high among participants (49.4%). HBcAb has been associated with a delay in HIV viral suppression to undetectable levels and poor HIV treatment outcomes in co-infected patients [36].

Among HBV/HIV co-infected participants, the presence of HBsAb was not significantly associated with coinfection status. Although more males (06) than females (02) were HBsAb positive, the association was insignificant. However, a significant association was obtained between the Age group and HBsAb. A study in Korea reported variations in the prevalence of HBsAb among participants according to birth year within different cohorts and among HIV study participants less than 30 years old. Despite implementing immunisation programs, it obtained an HBsAb prevalence of 58.1%, suggesting that HBsAb positivity does not persist in protective titers in PLHIV even after complete HBV vaccination [32].

HBeAg seropositivity in HBV/HIV coinfection was associated with liver enzyme levels: ALT ($P=0.043$) and AST ($P=0.039$). HBeAg positivity is a marker of HBV replication [37]. A study in Nigeria suggested that HBeAg

may be responsible for elevated ALT levels and that HBV infection causes changes in liver enzymes [38]. However, variants of HBV with pre-core and BCP mutation have led to an increasing incidence of HBeAg-negative chronic HBV with higher ALT levels than those with HBeAg-positive [39]. In this study, HBeAb ($P=0.001$) and HBcAb ($P=0.001$) were associated with region. HBeAb indicates HBeAg seroconversion or HBV treatment endpoint, and HBcAb implies current or past HBV infection [40]. It implies that HBV endemicity variations will likely affect both markers' prevalence. Although in this study, HBcAb was associated with ALT and AST levels, $P=0.001$ and $P=0.018$, respectively, Ikeda et al. argue that variations in ALT could be mainly a result of factors like high intake of alcohol or obesity rather than with HBV infection; thus, ALT cannot be used as a surrogate marker of HBV infection [41]. ALT was more likely to be associated with lifestyle factors. Therefore, ALT may be excluded as a surrogate marker of HBV.

Limitations of the Study

This study did not establish if participants had Hepatitis B before starting HIV treatment or while already on treatment. As a result, the incidence of HBV in people on antiretroviral treatment cannot be determined. Information on Viral load and CD4+ T-Lymphocyte counts was missing for some study participants, and this could introduce biased conclusions on associations with CD4+T-Lymphocyte counts and viral loads.

Conclusion

This study reported high HBV/HIV coinfection rate among study participants, further strengthening the need to routinely screen for HBV and its different sero-markers in PLHIV on antiretroviral treatment. This will improve the management of patients with HBV/HIV coinfection and reduce complications and mortality from liver disease in PLHIV.

What is Already known on this Topic?

The prevalence of Hepatitis B in PLHIV is higher than that of the general population.

HIV and Hepatitis B have similar modes of transmission.

What this Study Adds

It highlights the necessity for routine screening of Hepatitis B in people living with HIV, even on antiretroviral treatment with a Tenofovir-based regimen. It also estimates the HBV/HIV coinfection prevalence in people living with HIV on antiretroviral treatment in three regions of Cameroon, and findings from this study could strengthen policy implementation on routine HBV screening among HIV-infected persons attending care and treatment centres in Cameroon for routine follow-up and antiretroviral drug pick-up.

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Authors' Contribution

Sandrine Donfack Mewoabi Contributed to the research's conception, design and conduct. Valentine Ngum Ndze contributed to the design and review of the first draft of the manuscript, Njouendou Abdel Jelil, contributed to the statistical analysis, Theresa Nkuo-Akenji and Nguedia Jules Clement Assob Supervised the work. All authors read and approved the final manuscript.

Competing Interests

The authors declare no competing interests.

Data Availability

The primary research data collected from this study can be obtained by an email request to the corresponding author.

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