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Research article

Hepatitis B and C infections in HIV-1 patients on combination antiretroviral therapy (cART) in Ghana: implications for immunologic recovery, clinical response to treatment, and hepatotoxicity

Theophilus Benjamin Kwofie [a], Daniel Adigbli [b], James Osei-Yeboah [c], Emmanuel Ativi [c], Sylvester Yao Lokpo [c,*]

[a] Department of Microbiology and Immunology, School of Medicine, University of Health and Allied Sciences, Ho, Ghana
[b] Laboratory Department, Krachi-West District Hospital, Krachi, Ghana
[c] Department of Medical Laboratory Sciences, School of Allied Health Sciences, University of Health and Allied Sciences, Ho, Ghana

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ABSTRACT

Background: Viral hepatitis could have an impact on the treatment response in HIV patients. In this study, we sought to determine the prevalence of hepatitis B and C infections and examine the effect on the treatment response in HIV-1 patients attending antiretroviral therapy (ART) centers in the Volta and Oti Regions of Ghana.
Method: A longitudinal study design was employed. A cohort of 200 newly diagnosed HIV-1 positive adults who met the inclusion criteria (CD4 count ≤350 cells/μl) were enrolled at three ART Centers and initiated on the combination Antiretroviral Therapy (cART) from January 2014 to December 2015. Blood samples obtained from each participant were subsequently screened for the presence of hepatitis B surface antigen (HBsAg) and hepatitis C antibody. Out of the 200 study respondents recruited, 93 HIV mono-infected were randomly selected plus all 17 HIV co-infected were prospectively followed for twelve months. Using standard methods, three consecutive measurements of CD4 cells, haemoglobin, and liver enzymes [(aspartate aminotransferase (AST), alanine aminotransferase (ALT), and alkaline phosphatase (ALP)] as well as weight measurements were performed at baseline, six months and twelve months, respectively, after treatment initiation.
Result: The overall HIV-viral hepatitis sero-positivity was 8.5%. HBV and HCV co-infections were 7.0% and 1.5% respectively. Among HIV mono-infected CD4 cell count, haemoglobin, and weight significantly increased from baseline to the twelfth month while levels remained statistically comparable in the HIV co-infected patients. The levels of AST, ALT, and ALP were more pronounced (hepatotoxicity) in the HIV co-infected compared to the HIV mono-infected at various time points within the twelve month.
Conclusion: The frequency of HIV-hepatitis co-infection was high. This correlates with poor immunological outcome, clinical response to treatment and pronounced hepatotoxicity. The findings, therefore, underscore the need for regular screening of HIV patients for early detection and appropriate management.

1. Introduction

Globally, the human immunodeficiency virus (HIV) infection remains a pandemic and public health problem, although conscientious efforts have been made over the years to curb the menace. In 2018, an estimated 37.9 million people were infected with HIV, and out of this figure more than two-thirds occurred in sub-Saharan Africa [1]. The global prevalence of hepatitis B Virus (HBV) and hepatitis C Virus (HCV) infections among people living with HIV (PLWHIV) were estimated at 7.6% and 2.4%, respectively [2, 3]. A systematic review of the burden of viral hepatitis in HIV infection among Africans revealed HIV/HBV and HIV/HCV co-infection rates of 15% and 7%, respectively [4]. In Ghana, HBV infection is common in HIV individuals with rates as high as 13.5%, whereas about 3% of the HIV population are living with HCV infection [5, 6].

Previous studies have established that HIV co-existence with HBV or HCV infection could complicate the prognosis by hastening its progression to AIDS, inducing hepatic injury and impairing the ability to recover immunologically [7, 8, 9, 10]. However, those findings were met with contradictory reports from other studies [11, 12]. There is therefore lack

* Corresponding author.
E-mail address: sylvesteryao34@gmail.com (S.Y. Lokpo).

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of consensus on the role of viral hepatitis in the pathogenesis of HIV infection, necessitating the full understanding of the disease process through on-going studies. Moreover, due to the increased accessibility to the combination Antiretroviral Therapy (cART), [formerly referred to as Highly Active Antiretroviral Therapy (HAART)], there has been significant reduction in morbidity and mortality [13, 14], although hepatic diseases resulting from chronic HBV and HCV infections have been reported [15].

Prior to 2013, WHO recommended the initiation of antiretroviral therapy (ART) in adults with severe or advanced HIV clinical disease (clinical stage 3 or 4) or CD4 count ≤350 cells/μl [16]. However, the updated guidelines recommended treatment regardless of the clinical stage and CD4 cell count [16]. This eligibility criteria was largely retained in subsequent editions, although new recommendations were made to other aspects of the treatment guidelines [17, 18]. Also, in 2015, a combined therapy of Tenofovir (TDF)+Lamivudine (ETC) or Emtricitabine (FTC)+Efavirenz (EFV) was recommended as the preferred first line treatment, while Zidovudine (AZT) + 3TC + EFV or Nevirapine (NVP) or TDF + 3TC or FTC + Dolutegravir (DTG etc) were proposed as alternative first line treatment in the clinical setting [18]. It, however, emerged later that DTG use during conception was associated with neural tube defect. Hence, to ensure safety of the developing foetus, treatment with DTG was recommended only after the first trimester [19, 20, 21].

Moreover, TDF and FTC have been shown to inhibit hepatitis B viral activities, hence TDF and FTC based regimens are good candidates for the treatment of HIV-HBV co-infections [22]. With the increasing need for a more potent, and yet effective patient-centered outcome, however, the Direct-Acting Antivirals (DAAs) are currently the standard of care for chronic HCV infection [23].

In developing countries, including Ghana, the diagnosis, management, and monitoring of chronic viral hepatitis are not comprehensively integrated into the management of HIV/AIDS owing in part to logistical constraints [24, 25]. Besides, most healthcare workers manning ART centers are not adequately trained to provide specialized services to HIV patients with viral hepatitis. Hence, this lack of integrated management system has the potential to increase cases of treatment failures and even deaths among HIV patients.

In the Volta and Oti Regions, there is currently limited information on the burden of viral hepatitis and its impact on the management of PLWHA. Hence, using a longitudinal study design, we aimed to examine the prevalence and assess the effect of HBV and HCV infections on the treatment responses of HIV-1 patients receiving care at three ART centers who were monitored during a twelve month period.

2. Materials and methods

2.1. Study area and study site

A multi-center study involving three Anti-Retroviral Therapy (ART) centers at the Krachi-West District Hospital (KWDH), Hohoe Municipal Hospital (HMH), and the Ho Teaching Hospital (HTH) in the Volta and Oti Regions of Ghana was carried out from January 2014 to December 2015. The KWDH center provides services to clients in the Krachi West District located in the Oti Region while HMH and HTH sites render services in the Hohoe and Ho municipalities, respectively. Ho is the regional capital of the Volta Region and it serves as the major treatment center in the Volta Region. According to the 2010 population and housing census, the Ho municipality has an estimated population of 177,281 with 83,819 males and 93,462 females.

2.2. Study design and sampling technique

A longitudinal study design was employed where a study cohort of newly diagnosed HIV-1 positive adults were enrolled at the three ART Centers. Out of the 315 who tested positive to HIV-1 antibodies, 200 had CD4 counts of 350 cells/μl or less and were therefore eligible for enrollment onto the cART according to the recommended treatment protocols at the time. Also, out of the 200 HIV-1 participants who had been initiated on cART, 93 HIV mono-infected were randomly selected and all 17 HIV co-infected participants [17] were included for treatment monitoring for a period of twelve months.

2.3. Data collection

Patients attending the ART Centers for the purposes of clinical diagnosis (referred by clinicians) or voluntary testing (walk-in) had their blood samples drawn and screened first for HIV-1 antibodies using the HIV First Response Test Card 1–2.0 (Premier Medical Corporation Ltd, India), a rapid diagnostic test kit. Supplementary tests were performed on all reactive samples using a second rapid test kit (Oraquick Rapid HIV– 1/2, OraSure Technologies Inc, USA) following the WHO testing protocols for HIV testing and the algorithm of the National AIDS Control Programme [18]. For each eligible patient, biographic data and other relevant information necessary for assessing the possible risk of co-infection with HBV or HCV were collected. Three consecutive blood samples were obtained for the measurement of CD4 cells, haemoglobin, and liver enzyme including aspartate aminotransferase (AST), alanine aminotransferase (ALT), and alkaline phosphatase (ALP), as well as weight at baseline, six months and twelve months after treatment initiation. However, patients who admitted chronic alcohol use, and those who were pregnant were excluded from this study.

2.4. Blood sampling

About 10 ml of whole blood sample was collected from each participant and out of that, 5 ml was dispensed into sterile BD vacutainer tubes containing ethylene-diamine-tetra-acetic acid (EDTA). The anti-coagulated blood was thoroughly mixed and used to estimate CD4 cell count and hemoglobin levels. The remaining 5ml blood in the BD serum separator gel tube was centrifuged at 3000rpm for 2 min to obtain serum. The serum was used to detect the presence of HBsAg) and ant-HCV as well as to measure the levels of liver enzymes.

2.5. HBV and HCV screening

The samples were tested for the presence of HBsAg (bio Merieux, France) and anti-HCV (Flavicheck-HCV Qualpro Diagnostics, India) using the enzyme immunoassay based rapid test kits. For HBsAg testing, a drop (40μl) of serum was dispensed onto the specimen pad of the test strip and a drop (40μl) of buffer was added. Anti-HCV was tested by adding two drops (60–80μl) of serum onto the test pad and two drops (50μl) of diluting buffer. In both cases, results were read after 15 min as positive test results indicating two red visible bars in the control and patients windows of the test strip while only one bar in the control window indicated negative results.

2.6. Determination of CD4 cell count, liver enzymes, and haemoglobin levels

The CD4 cell count was measured on an automated machine (BD FACSCount) based on the principle of flow cytometry. AST, ALT, and ALP were measured on a fully automated chemistry analyzer (Vitalab Selectra Junior, Germany). Haemoglobin levels were estimated using the Sysmex KX21N analyzer (Sysmex Corporation, Kobe, Japan). All variables were measured using methods predefined by the reagent manufacturers.

2.7. Measurement of weight

The body weight of each patient was weighed to the nearest 1.0 kg in light clothing, without shoes using a bathroom scale (Seca Medical Measuring Systems and Scales, Humburg).

2.8. Anti-retroviral treatment initiation and monitoring

The WHO recommendations on the initiation of ART were followed: HIV-1 positive patients with CD4 cell count <350 cells/μL or its equivalent WHO staging III & IV were eligible and therefore placed on cART. A first-line standard combination regimen comprising zidovudine (300mg), lamivudine (150mg), and nevirapine (200mg) was served at baseline. In the case of contraindications to zidovudine or nevirapine, tenofovir (300mg) or efavirenz (600mg) was administered. Participants presenting with haemoglobin levels of 8 g/dl or above were initiated on zidovudine, lamivudine, and nevirapine. Participants whose haemoglobin levels were less than 8 g/dl at the time of recruitment (4 subjects) or those who developed severe anaemia (3 subjects) during the above-mentioned regimen were given a combination regimen of tenofovir, lamivudine, and nevirapine. See Table 1. In limited instances, drug combination was based on availability. Hepatitis co-infection was not considered in the choice of drugs simply because the hepatitis status of the patients was unknown to the healthcare providers during the study period. However, adherence assessment was based on pill counts and patients' self-report at every visit.

2.9. Definition of outcome variables

Immunologic response was defined by the average changes in CD4 cell counts from baseline through to the twelfth month. Clinical response to treatment was assessed based on the average changes in body weight and haemoglobin levels from the start of treatment to the twelfth month. Hepatotoxicity was defined as elevated levels of transaminases (ALT, AST, and ALP) from baseline values through to the twelfth month.

2.10. Data analysis

The normality of all continuous variables was tested. Continuous variables were expressed as their mean ± SD, whereas categorical variables were expressed as figures and proportions. The comparison of the mean of hepatitis positive and negative individuals was performed using the unpaired student t-test. Paired analysis of variance and Bonferroni

Table 1. Socio-demographic characteristics, viral hepatitis co-infection profile, and risk factors among HIV-1 Patients in the Volta and Oti Regions.

Parameter	HIV-1 Only	HIV-Hepatitis Co-infection
Total	200 (100.00)	17 (8.50)
Age (years)		
≤30	42 (21.00)	6 (35.28)
31–40	69 (34.50)	5 (29.40)
>40	89 (44.50)	6 (35.28)
Gender		
Male	60 (30.00)	4 (23.56)
Female	140 (70.00)	13 (76.44)
Marital Status		
Single	95 (47.50)	7 (41.20)
Married	105 (52.50)	10 (58.80)
Educational Background		
No Education	47 (23.50)	5 (29.40)
Basic	84 (42.00)	8 (47.08)
Secondary	45 (22.50)	2 (11.76)
Tertiary	24 (12.00)	2 (11.76)
Employment Status		
Unemployed	54 (27.00)	6 (35.28)
Informal Sector	110 (55.00)	9 (52.96)
Formal Sector	36 (18.00)	2 (11.76)
Area of Residence		
Urban	114 (57.00)	11 (64.72)
Rural	86 (43.00)	6 (35.28)
Hepatitis status		
HBV infected	14 (7.00)	3 (17.64)
HCV infected	3 (1.50)	14 (82.36)
Sharing sharps		
Ever	-	11 (64.72)
Never	-	6 (35.28)
Transfusion Status		
Ever	-	3 (17.64)
Never	-	14 (82.36)
cART Initiation		
AZT+3TC + NVP	179 (91.30)*	17 (8.70)*
TDF+3TC + NVP	4 (2.00)	-
cART Regimen Switch		
TDF+3TC + NVP	3 (1.53)*	-

Data are presented as the frequency with proportion in parenthesis. AZT-Zidovudine, 3TC-Lamivudine, TDF-Tenofovir, EFV-Effavirenz, NVP-Nevirapine * denotes 196 was used as the denominator.

posthoc test was used to compare mean variables for baseline, month six, and month twelve. A comparison of trend in the categorical outcomes was performed using a Chi-square test for trends. The level of significance was considered at a p-value less than 0.05.

2.11. Ethical approval

The Committee on Human Research and Publication Ethics of the School of Medicine and Dentistry, Kwame Nkrumah University of Science and Technology, Kumasi, Ghana approved for the study to be undertaken (Ethical Clearance Ref No: CHRPE/AP/012/14). Permission was also sought and obtained from the management of the selected hospitals. A written informed consent form was obtained from each participant. Participants were fully informed about the purpose, procedures, risks, and benefits of participating in this study. Each participant was assured of the confidentiality of their response.

3. Results

Out of 200 HIV-1 respondents recruited in this study, the majority (70%) were females. The average age was 39 years, ranging from a minimum of 18–68 years. More than 52% were married. Thirty-four percent of the respondents had attained at least secondary level education at the time of this study. The majority were gainfully employed (73%), working in the informal sector (55%), and earning low-income (66.5%). More than half (57%) were residents in urban areas. No intravenous drug users (IVDU), prostitution, and men who had sex with men (MSM) were enrolled in this study. See Table 1 below.

The overall viral hepatitis co-infection was 8.5%. Seven percent (7%) tested positive to HBV while 3 (1.5%) were positive to HCV. However, none of the respondents recorded triple infections. Viral hepatitis co-infection was descriptively higher among females (9.29%) and the married (9.52%). The frequency of co-infection was highest in respondents without formal education, unemployed, and urban dwellers (9.65%) as well as those who had ever experienced blood transfusion (15.79%) and had ever shared sharps (8.94%). See Table 1 below.

Among the HIV mono-infected, appreciable levels of CD4, weight, and haemoglobin were observed from baseline to the twelfth month of treatment. However, the HIV co-infected presented no significant change in the aforementioned variables. In the case of CD4 levels, the two groups presented with comparable levels at baseline, but the HIV mono-infected recorded significantly higher CD4 levels after six months and at the twelfth month of therapy compared to the HIV co-infected. Weight gain among the HIV mono-infected was significantly increased compared to the HIV co-infected. Haemoglobin concentration was comparable between the two groups of HIV patients at baseline through to the first six months of therapy. However, the HIV mono-infected presented with significantly higher haemoglobin levels at the end of the twelfth month of treatment. No significant change in the levels of enzymes among the two groups was observed during the period of the study. See Table 2.

Among the HIV mono-infected, significantly higher levels of CD4, weight, and haemoglobin were observed from baseline to the twelfth month of therapy. In contrast, HIV co-infected showed no significant increase in CD4, weight, and haemoglobin levels throughout the twelve months of therapy. No significant changes in the concentrations of the three liver enzymes assayed in this study were seen. See Table 3.

Respondents who did not present with HCV co-infection exhibited significant additive levels of CD4, haemoglobin, and weight during the period of therapy while those co-infected with HCV showed no significant change in CD4, weight, and haemoglobin levels at the end of the twelfth month of therapy, though no significant difference was observed at the baseline of treatment. See Table 4.

As seen in Figure 1A, at the initiation of therapy, 47.27% and 52.73% of the respondents clustered at CD4 levels less than 200 and from 200 to 500 respectively. The cluster distribution among the HIV-mono-infected and co-infected was comparable at baseline and after six months of therapy (Figure 1A, B). There was a significant shift in cluster distribution across the three different CD4 categorizations at the twelfth month of treatment experience between the HIV co-infected and their mono-infected counterparts (p-0.0006). Among the co-infected, 52.94% clustered below 200 and the rest at 200 to 500, with none presenting with CD4 cell count more than 500 cells/ml. For the HIV mono-infected 26.88% had CD4 levels more than 500 cells/ml, with 58.06 clustering between 200 and 500 cells/ml and 20.91% clustering below the 200 cells/ml. Figure 1C.

4. Discussion

The overall viral hepatitis sero-positivity (8.5%) in our study cohort of HIV-1 patients was high. HBV and HCV co-infections were 7.0% and

Table 2. Treatment outcome among HIV seropositive receiving cART at the ART Centers stratified by HBV-HCV infection status.

Parameter		Baseline	Month-6	Month-12	*p-value*
CD4 count (cells/ml)	Hepatitis –Negative	130.59 ± 3.35	250.21 ± 1.8	333.73 ± 1.664	*<0.0001*
	Hepatitis-Positive	152.69 ± 2.59	150.24 ± 2.12	181.43 ± 1.854	*0.7417*
	p-value	*0.6148*	*0.0022*	*<0.0001*	
Weight (kg)	Hepatitis –Negative	56.18 ± 8.54	59.02 ± 8.1	60.46 ± 8.086	*0.0018*
	Hepatitis-Positive	58.88 ± 11.36	59.94 ± 11.12	59.29 ± 8.964	*0.9573*
	p-value	*0.2585*	*0.6864*	*0.5912*	
Haemoglobin (g/dl)	Hepatitis –Negative	11.00 ± 1.97	11.57 ± 1.75	12.25 ± 1.287	*<0.0001*
	Hepatitis-Positive	10.64 ± 1.9	10.93 ± 1.38	10.93 ± 1.572	*0.8388*
	p-value	*0.4832*	*0.1581*	*0.0003*	
ALT conc (U/L)	Hepatitis –Negative	23.18 ± 10.07	25.81 ± 12.93	27.04 ± 12.445	*0.0792*
	Hepatitis-Positive	29.06 ± 9.97	33.76 ± 12.14	31.12 ± 11.837	*0.4855*
	p-value	*0.0289*	*0.0204*	*0.2140*	
AST conc (U/L)	Hepatitis –Negative	26.25 ± 10.95	28.39 ± 11.91	27.68 ± 10.089	*0.4031*
	Hepatitis-Positive	25.82 ± 9.28	30.12 ± 10.87	29.06 ± 8.785	*0.4106*
	p-value	*0.8811*	*0.5783*	*0.5981*	
ALP conc (U/L)	Hepatitis –Negative	78.19 ± 29.65	85.66 ± 30.72	80.19 ± 21.165	*0.1618*
	Hepatitis-Positive	69.12 ± 25.37	74.59 ± 25.94	72.29 ± 22.494	*0.8104*
	p-value	*0.2389*	*0.1656*	*0.1639*	

Data are presented as mean ± standard deviation. p-value is significant at 0.05. ALT-Alanine aminotransferase, AST-Aspartate aminotransferase, ALP-Alkaline phosphatase.

Table 3. Treatment outcome among HIV-1 participants receiving cART at the ART Centers stratified by HBV infection status.

Parameter		Baseline	Month-6	Month-12	*p-value*
CD4 count (cells/ml)	HBV-Negative	132.07 ± 3.31	248.08 ± 1.81	329.99 ± 1.67	*<0.0001*
	HBV-Positive	146.22 ± 2.73	142.89 ± 2.17	172.07 ± 1.88	*0.8079*
	p-value	*0.7625*	*0.0023*	*<0.0001*	
Weight (kg)	HBV-Negative	56.54 ± 8.71	59.44 ± 8.31	60.66 ± 8.06	*0.0025*
	HBV-Positive	57.00 ± 11.31	57.29 ± 10.39	57.71 ± 8.94	*0.9830*
	p-value	*0.8600*	*0.3831*	*0.2110*	
Haemoglobin (g/dl)	HBV-Negative	10.95 ± 1.97	11.52 ± 1.75	12.17 ± 1.34	*<0.0001*
	HBV-Positive	10.93 ± 1.98	11.13 ± 1.43	11.19 ± 1.61	*0.9143*
	p-value	*0.9727*	*0.4278*	*0.0142*	
ALT conc (U/L)	HBV-Negative	23.40 ± 10.01	26.42 ± 13.25	27.52 ± 12.61	*0.0503*
	HBV-Positive	28.86 ± 10.9	31.29 ± 11.42	28.71 ± 11.08	*0.7911*
	p-value	*0.0619*	*0.1947*	*0.7380*	
AST conc (U/L)	HBV-Negative	26.31 ± 10.81	28.90 ± 12.1	28.07 ± 10.21	*0.2573*
	HBV-Positive	25.29 ± 9.93	27.00 ± 8.91	26.64 ± 7.29	*0.8623*
	p-value	*0.7382*	*0.5745*	*0.6149*	
ALP conc (U/L)	HBV-Negative	78.74 ± 29.39	86.34 ± 30.68	80.93 ± 21.27	*0.1434*
	HBV-Positive	63.43 ± 23.95	67.50 ± 20.74	65.57 ± 18.27	*0.8782*
	p-value	*0.0657*	*0.0285*	*0.0117*	

Data are presented as mean ± standard deviation. A p-value is significant at 0.05. ALT-Alanine aminotransaminase, AST-Aspartate aminotransaminase, ALP-Alkaline phosphatase.

Table 4. Treatment outcome among HIV seropositive receiving cART at the ART Centers stratified by HCV infection status.

Parameter		Baseline	Month-6	Month-12	*p-value*
CD4 count (cells/ml)	HCV-Negative	132.53 ± 3.26	232.54 ± 1.9	305.98 ± 1.77	*<0.0001*
	HCV-Positive	186.90 ± 2.2	189.93 ± 2.05	232.27 ± 1.78	*0.9154*
	p-value	*0.6182*	*0.5922*	*0.4102*	
Weight (kg)	HCV-Negative	56.29 ± 8.89	58.79 ± 8.4	60.10 ± 8.21	*0.0042*
	HCV-Positive	67.67 ± 7.77	72.33 ± 2.89	66.67 ± 4.93	*0.4604*
	p-value	*0.0306*	*0.0065*	*0.1723*	
Haemoglobin (g/dl)	HCV-Negative	10.99 ± 1.97	11.51 ± 1.71	12.11 ± 1.37	*<0.0001*
	HCV-Positive	9.30 ± 0.53	10.00 ± 0.7	9.73 ± 0.64	*0.4383*
	p-value	*0.141*	*0.1321*	*0.0036*	
ALT conc (U/L)	HCV-Negative	23.93 ± 10.31	26.52 ± 12.83	27.26 ± 12.24	*0.0977*
	HCV-Positive	30.00 ± 4.58	45.33 ± 9.29	42.33 ± 9.71	*0.1284*
	p-value	*0.313*	*0.0134*	*0.0371*	
AST conc (U/L)	HCV-Negative	26.12 ± 10.78	28.21 ± 11.54	27.54 ± 9.75	*0.3488*
	HCV-Positive	28.33 ± 6.03	44.67 ± 6.66	40.33 ± 6.35	*0.0468*
	p-value	*0.7249*	*0.0158*	*0.0262*	
ALP conc (U/L)	HCV-Negative	76.26 ± 29.3	83.28 ± 30.16	78.28 ± 21.31	*0.1534*
	HCV-Positive	95.67 ± 11.68	107.67 ± 24.38	103.67 ± 9.29	*0.6802*
	p-value	*0.2566*	*0.1687*	*0.0428*	

Data are presented as mean ± standard deviation. p-value is significant at 0.05. ALT-Alanine aminotransferase, AST-Aspartate aminotransferase, ALP-Alkaline phosphatase.

1.5% respectively (Table 1). This high HBV infection rate corroborates findings of previous studies among PLWHIV in the Eastern (8.8%) [26] and Central regions of Ghana (6.1%) [27] as well as those of other African countries [28, 29, 30, 31], but slightly lower than values obtained in other parts of the country [6, 32, 33, 34, 35]. The HCV co-infection rate also compares with previous works among Zambians (2.2%) [36] and Nigerians (1.6%) [29]. The result is, however, lower than the 5.5% reported in Kumasi [32], and 4.2–10.3% among Kenyans [37, 38]. The relatively low HCV positive cases in our study could be linked to the low transfusion rates and non-existence of Intravenous Drug Users (IVDU) among the study respondents. These are major risk factors responsible for the transmission of HCV infection among HIV patients [39, 40, 41]. Moreover, blood is screened for viral hepatitis before they are issued out by clinical laboratories and coupled with the fact that IVDU is a western lifestyle and therefore alien to our region. However, we did not identify any of the participants to have presented with triple infection, which is also consistent with earlier studies in Ghana [27], Ethiopia [42], and Nigeria [30, 43].

Importantly, even with the relatively simple, rapid diagnostic tests employed in this study, with no proof of active viral replications, a trend to significant differences was observed between individuals infected with HIV alone, and those showing positive tests to HCV or HBV. Thus, we found a trend towards increasing CD4 cells, haemoglobin, and weight levels among the HIV mono-infected while levels remained comparable among HIV co-infected from baseline to the twelfth month of treatment whether taken together (Table 2), or analysed separately, a rapid test for

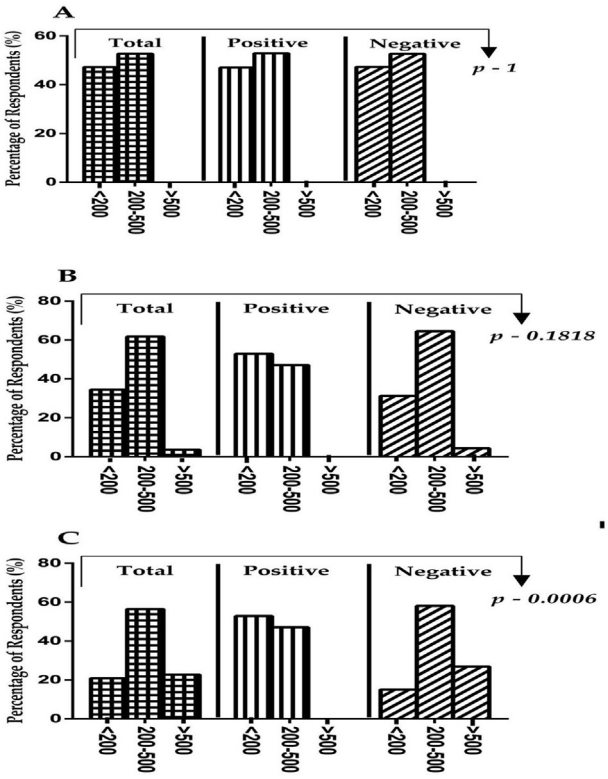

Figure 1. Respondent CD4 clusters stratified by viral co-infection status. A-Baseline, B- Month six and C-Month twelve.

either HBV (Table 3) or HCV (Table 4). In addition, HIV mono-infected had the tendency to cluster at high CD4 cell counts compared to their HIV co-infected counterparts in the twelfth month of treatment (Figure 1C). This apparent failure to recover immunologically, improve haemoglobin and weight levels among the HIV co-infected could be attributed to the synergistic effect of HIV and HBV or HCV infections.

Similar findings of negative immune recovery have been reported among HIV co-infected patients in other African countries [42, 44]. However, the sustained increases in the CD4+ cell count among the HIV mono-infected is reflective of a positive immunological outcome to therapy, which is also consistent with a previous report in Ghana [45]. Postulated mechanisms underlying HIV-HCV/HBV co-infections include HCV proliferation and the suppression of T helper cells [46, 47, 48], whereas HBV infection is associated with increased T-cell apoptosis [49]. Moreover, the improvement in weight observed among the HIV mono-infected in our study was similarly demonstrated by Ohene and colleagues who found increases in weight levels after therapy was initiated [45].

The lower average levels of haemoglobin generally observed among the HIV co-infected could be due to the destructive effect of HIV on the haemopoietic cell system, which may even worsen in the presence of viral hepatitis [50, 51]. Moreover, Zidovudine is also known to confound the incidence of anaemia via similar mechanisms resulting in the decline of haemoglobin levels in HIV patients [52, 53]. Notwithstanding, chronic HCV and HBV infection have been proposed to induce auto-immune and non-immune hemolytic syndrome, respectively [54, 55, 56].

Hepatotoxicity is associated with ARV use and it is responsible for the increased morbidity and mortality in HIV-infected individuals [57, 58]. Patients on ART with underlying viral hepatitis are more likely to experience organ toxicities including that of the liver [59, 60]. The higher levels of liver enzymes (AST, ALT, and ALP) observed among the HIV co-infected could suggest possible injury to the liver. The findings are consistent with Kalyesubula et al., (2011) [61] and Wondimeneh et al., (2013) [42]. The HIV is thought to infect hepatic cells, inducing injury to the liver, leading to fibrosis and raised liver enzymes; the injury process could further heighten in the presence of HBV and HCV infections [42, 62].

It is important to mention that the interpretation of the study findings should be made in the light of the following limitations: Firstly, we could not measure the viral load for both HIV and viral hepatitis (B and C) owing to logistical constraints. Secondly, the diagnoses of HIV and viral hepatitis infections were based on results of rapid diagnostic tests which only indicates that an individual has ever experienced an infection but not that the individual is experiencing active virus replication. Thirdly, we could not assess participants' nutritional status as this could have influenced their weight and immune statuses.

5. Conclusion

This study confirms an overall high prevalence of viral hepatitis among HIV-1 patients in the Volta and Oti Regions of Ghana. This could have implications for immunologic recovery, clinical response to treatment, and hepatotoxicity. The study findings, therefore, underscore the need for regular screening of HIV patients for early identification and appropriate management.

Declarations

Author contribution statement

Theophilus Benjamin Kwofie: Conceived and designed the experiments; Wrote the paper.

Daniel Adigbli: Conceived and designed the experiments; Performed the experiments; Contributed reagents, materials, analysis tools or data; Wrote the paper.

James Osei-Yeboah: Analyzed and interpreted the data.

Emmanuel Ativi, Sylvester Yao Lokpo: Analyzed and interpreted the data; Wrote the paper.

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Data availability statement

Data will be made available on request.

Competing interest statement

The authors declare no conflict of interest.

Additional information

No additional information is available for this paper.

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