ORIGINAL ARTICLE

# HEPATITIS C VIRUS (HCV) SEROPOSITIVITY IN A COHORT OF HIV CO-INFECTED ART NAÏVE SUBJECTS: ASSESSMENT OF BIOCHEMICAL PROFILE

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## ABSTRACT

**Background:** Hepatotropic virus infection, such as Hepatitis C Virus (HCV) infection is altering the gains of highly active Antiretroviral therapy HAART; and rapidly increasing non-AIDS-related mortality in people living with HIV disease.
**Aim:** This warranted the investigation of some biochemical indices in a Cohort of 94 HIV Seropositive Subjects, out of which 11 were co-infected with HCV. Controls consisted of 80 subjects Seronegative for HIV and HCV antibodies.
**Method:** We analysed Aspartate Transaminase (AST), Alanine transaminase (ALT), Alkaline Phosphatase (ALKP), Creatinine, Total Cholesterol (TCH), Random Blood Glucose (RBG) and Potassium (K+) in the HIV, HIV/HCV and HCV subjects and the controls.
**Result:** The liver enzymes mean values (AST, ALT, ALP) were significantly higher in the HIV/HCV subjects compared to the HIV, HCV mono-infections and the controls ($P<0.01$). Similarly, Creatinine mean value was also higher in the HIV/HCV compared to the other studied groups ($P< 0.001$). Total cholesterol (TCH) and potassium (K+) were incomparable in the studied groups ($P> 0.05$). Conversely, random blood glucose showed a significant difference in the mean values with the highest value registered in the HIV/HCV subjects ($P<0.05$).
**Conclusion:** HIV/HCV Co-infection may worsen the biochemical profile in HIV setting, and may increase non-AIDS-related morbidity and mortality in people living with HIV disease. Understanding the scope of this phenomenon, in addition to rapid interventional measures may be necessary to ameliorate its impact.

**KEYWORDS:** HCV, HIV, Co-infection, Biochemical indices

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## INTRODUCTION

A hepatic disease has emerged as a major cause of morbidity and mortality in the HIV/AID setting, particularly in the post-antiretroviral therapy (ART) era[1]. While ART has substantially extended the life expectancy of HIV-infected persons, hepatitis B virus and hepatitis C virus (HCV) have become a leading cause of non-AIDs-related deaths among people living with HIV[2,3,4].

HIV/HCV co-morbidity is believed to synergistically assault hepatic architecture leading to accelerated progression to variable hepatic diseases including metabolic dysfunction, cirrhosis, hepatocellular carcinoma[2,5] and ART-related hepatotoxicity[6].

The driving force for this co-infection is hinged on the fact that HIV and Hepatotropic viruses share similar principal routes of transmission[1, 2]. However, hepatitis C virus (HCV) transmission in largely associated with non-sexual parenteral routes including percutaneous exposure to intravenous drug use (IDU) exposure to blood and blood products[7-11].

Sub-Saharan Africa with a high burden of HIV infection accounts for about 19% of global HIV/HCV co-infection[1, 12]. The reported co-infection rate in our environment was comparably low[7, 8]. However, in a study in another part of Northern Nigeria, a rate not less than 8.2% was documented[11].

Literature evidence suggested that HIV infection modifies the natural history of HCV morbidity by speeding up the liver histological alteration leading to end-stage hepatic disease in a shorter time [13, 14].

Multiple mechanisms were suggested to explain the accelerated morbidity; these include–HIV increasing HCV replication, augmenting HCV-induced hepatic inflammation, increases hepatocyte apoptosis, increase microbial translocation from the gut leading to impaired HCV-specific immune responses[15]. Falade et al.,[5] asserted that liver-related mortality is 2 times higher for chronic HCV/HIV co-infection in the setting of CD4+ cell counts <200 cell/µL compared to counts > 350cells/µl.

The consequences of HIV/HCV co-morbidity were related to certain metabolic dysfunctions including insulin resistance, diabetes, renal insufficiency and hepatic enzymes derangement[16, 17, and 18]. We are not aware of a targeted study on the impact of HIV/HCV on biochemical profiles of patients in North-Eastern Nigeria; we, therefore, considered it necessary to contribute some information on this subject.

## MATERIALS AND METHODS

This is a retrospective cohort study conducted at University of Maiduguri Teaching Hospital (UMTH) from September 2013 to January 2015. Prospecting blood donors 94 in number, confirmed to be seropositive for human immunodeficiency virus (HIV) infection by western blots technique were recruited. Eleven (11) of the participants were co-infected with HIV and hepatitis C virus (HCV); 12 HCV mono-infected were also enlisted. In addition, participants' seronegative for HIV, HCV and HBV 80 in number was enlisted as controls.

Out of 8ml of blood collected from each participant, 2ml was dispensed into EDTA plastic blood bottle for CD4+ T-cell counts cytoflow technique, 2ml into fluoride oxalate bottle for Random blood glucose (RBG), while 4ml was allowed to clot in a plain blood bottle and serum separated immediately by centrifugation at 3000g for 5 minutes and used for Aspartate transaminase (ASP), Alanine transaminase (ALT), Alkaline Phosphatase (ALP), Creatinine (Creat), Total cholesterol (TCH), and Potassium (K+) using, Biochemical auto analyzer model, Hitachi-Cobas G311 leumes S/N 46-02 (Cobas Roche GMbH – D68298 Mannheuim) and reagent kits from the same company. HCV was confirmed by ELISA technique using a kit from DIA PRO Diagnostic Bio probes 2009g Sesto San Giovanni (Milano)-Italy.

HIV screening was carried out with an immune chromatographic kit (Chambio HIV 1-2 STAT-PAK). Positive samples were confirmed by western blotting (Qualicode™ HIV 1 and 2 kits).

## RESULTS

We enlisted a total of 186 participants, males were 128 (68.8%) and females 58 (31.2%). The participants were distributed as follows; HIV mono-infected participants 83(44.6%), HIV/HCV co-infected participant 11(5.9%); HCV 12 (6.5) controls 80 (43.0%). The controls were HIV, HCV, HBV seronegative and apparently health blood donors (see table I).

Table II depicts the age distribution of the participants; a majority of whom fall into the age groups (16-26) and (27-37). The prevalence of HIV infection appeared to decrease with age with 6.5% at ages 49-59. Similar age distribution was also observed in HIV/HCV Co-morbidity subjects who stood at 0.5% for the same age groups.

Table III displays the mean (±SD) CD4 T cells count. The lowest mean count was observed in the HIV/HCV (176.40 ± 22.30) in contrast to HIV single infection 220.18 ± 41.34. As expected the mean count was highest for control participants 614.15 ± 120.30.

The mean (± SD) values of biochemical parameters of the studied population are shown in table IV; mean values of aspartate transaminase (AST), alanine transaminase (ALT) and alkaline phosphates (ALP) in the HIV groups were increased compared to the controls (P<0.01). However, these liver enzymes were more efficient in the HIV mono-infection compared to the HIV/HCV co-infection (P< 0.001). Similarly, creatinine was more elevated in the HIV/HCV co-morbidity compared to the HIV mono (P<0.01) and the controls (P< 0.001). RBG was not comparable between the control and HIV single infection (P = 0.421). But there is a significant increase in the HIV/HCV co-infection compared to HIV mono-infection and the control (P< 0.001). TCH and $K^+$ were also incomparable across studies groups (TCH= 1 Vs 2 P = 0.174, 1 Vs 3 P = 0.310; 2 Vs 3 P = 182) (RBG= 1 Vs 2 P = 0.134; 1 Vs 3 P= 0.132; 2 Vs 3 P = 0.121).

Comparison of the mean values of these biochemical parameters between HIV/HCV and HCV participants reveals more efficient liver enzymes, RBG and Creatinine in the HCV mono-infection while TCH and K+ remained incomparable see table V.

**Table I: Gender distribution of all subjects**

| | CONTROL | | HIV | | HCV | | HIV/HCV | | TOTAL |
|---|---|---|---|---|---|---|---|---|---|
| | N | % | N | % | N | % | N | % | % |
| MALE | 57 | 30.6 | 56 | 30.1 | 07 | 3.8 | 08 | 4.3 | 128 68.8 |
| FEMALE | 23 | 12.4 | 27 | 14.5 | 05 | 2.7 | 03 | 1.6 | 058 31.2 |
| TOTAL | 80 | 43.0 | 83 | 44.6 | 12 | 6.5 | 11 | 5.9 | 186 100 |

**TABLE II: Age Distribution of all subjects**

| AGE GROUP | CONTROL | HIV | HCV | HIV/HCV | TOTAL |
|---|---|---|---|---|---|
| | N % | N % | N % | N % | |
| 16-26 | 26 (14.0) | 24 (12.9) | 4 (2.2) | 3(1.6) | 57 (30.6) |
| 27 – 37 | 22 (11.8) | 27 (14.5) | 6(3.2) | 5(2.7) | 60 (32.3) |
| 38 – 48 | 17 (09.1) | 20 (10.8) | 1(0.5) | 2(1.1) | 40 (21.5) |
| 49 – 59 | 15 (08.1) | 12 (06.5) | 1(0.5) | 1(0.5) | 29 (15.6) |
| TOTAL | 80 (43.0) | 83 (44.6) | 12(6.4) | 11(5.9) | 186(100) |

**TABLE III: Mean (±SD) of CD4+ T Count for all Subjects**

| VARIABLE | CONTROL | HIV | HIV/HC | F. STATISTICS | P.VALUE |
|---|---|---|---|---|---|
| $CD4^{+}$T Count (Cells/μL) | 614.15±120.30 | 220.18±41.34 | 176.40±22.30 | 73.32 | 0.001 |

**TABLE IV: Mean (± SD) Biochemical Parameters of All Subjects.**

| SUBJECTS | AST | ALAT | ALP | CREAT | RBG | TCH | K+ |
|---|---|---|---|---|---|---|---|
| 1. Control | 14.7 ± 11.56 | 21.0 ± 9.46 | 71.31 ± 21.53 | 43.11 ± 15.36 | 5.1 ± 0.30 | 4.5 ± 1.2 | 3.8±1.0 |
| 2. HIV | 24.33±6.3 | 26.8 ± 6.3 | 70.15 ± 21.0 | 91.7 ± 16.0 | 5.4 ± 1.3 | 4.1 ± 1.3 | 3.4±0.3 |
| 3. HIV/HCV | 68.9 ± 10.6 | 37.6 ± 4.3 | 101.70 ± 10.3 | 120.2 ± 1.9 | 8.78± 2.3 | 5.1 ± 3.4 | 3.1±0.7 |
| F. Statistics | 41.75 | 23.45 | 93.45 | 78.67 | 17.34 | 0.670 | 0.343 |
| p Value | 0.000*** | 0.00** | 0.00** | 000*** | 000*** | 0.341 | 0.413 |
| 1Vs 2 p Value | 0.01* | 0.101 | 0.310 | 000*** | 0.421 | 0.174 | 0.134 |
| 1. Vs 3 p Value | 0.00** | 0.04* | 0.00** | 0.000*** | 0.00** | 0.310 | 0.132 |
| 2Vs 3 p value | 0.00** | 0.01* | 0.00** | 0.00** | 0.00** | 0.182 | 0.121 |

Key: AST = Aspartate transaminase; ALAT = Alanine transaminase; ALP = Alkaline phosphatase; CREAT = Creatinine; RBG = Rand Blood Glucose.; TCH = Total Cholesterol, K+ = Potassium; *P Value* *** = 0.001; ** = 0.01; * = 0.05*

**Table V: Mean Biochemical Parameters of HCV nad HIV/HCV Participants**

| Subjects | AST | ALT | ALP | Creat. | RBG | TCH | K+ |
|---|---|---|---|---|---|---|---|
| HCV | 59.9±8.6 | 28.5±2.4 | 93.7±8.4 | 104.3±1.0 | 6.5±1.4 | 5.4±2.3 | 3.5±0.6 |
| HCV/HIV | 68.9±10.6 | 37.6±4.3 | 101.7±10.3 | 120.7±1.9 | 8.78±2.3 | 5.1±3.4 | 3.1±0.7 |

## DISCUSSION

Only 11(5.9%) of the studied participants were seropositive for HCV/HIV antibodies, while 83 (44.6%) were seropositive for HIV mono-infection. All were heterosexually active with a good number confessing multiple sex partnering. Those seropositive for HCV antibody did not refute frequent exposure to intravenous injections from informal health care facilities. This scenario appears to support the assertion that HCV is more efficiently transmitted by non-sexual parenteral routes[12, 15]. Mathew *et. al.,*[12] had opined that iatrogenic practice was a more common mode of HCV transmission in sub-Saharan Africa via the reuse of syringes and needles or inadequately screened blood/products.

In our study mean CD4 count was significantly lower in the HCV/HIV participants compared to the HIV mono-infected participants. This finding corroborated the studies that linked occurrence of this co-infection to the severity of HIV disease as evidenced by depletion of CD4 cell counts[3, 12, 15].

Liver enzymes AST, ALT ALP mean values were significantly higher in HIV/HCV co-infected participants compared to the HIV mono-infection and control group, these enzymes were also more efficient in HCV mono-infected participants.

A significant increase in the serum liver enzymes had been reported in previous studies[19,20]. Liver transaminases are useful

biomarkers of liver injury in individuals with some degree of intact liver function. Most liver diseases often cause only mild symptoms initially but it is important that these diseases are detected early to prevent complications[19].

ALT is found in serum and in various body tissue but is largely associated with the liver. It catalyses the transfer of an amino group from alanine to a-Ketoglutarate[19]. Raised serum ALT concentration is a strong reflection of hepatocellular damage or liver dysfunction[22]. Literature has revealed an association between HCV infection and insulin resistance. This is believed to be due to an increase in pro-inflammatory state and increase in cytokines such as tumour necrosis factor alpha (TNF) and interleukin 6. The ultimate result is abnormal lipid metabolism and subsequent deposition in the hepatocytes leading to hepatosteatosis[23].

Random blood glucose mean value was incomparable between the controls and the HIV mono-infection in this study. However, HIV/HCV participant's RBG mean value was significantly higher than the mean values for HIV, HCV mono-infections and the controls. RBG mean value in HCV mono-infection although higher than that in the controls was more efficient in comparison with the HIV/HCV co-infection. Hepatitis C disease was associated with auto-immune pancreatic beta-cell damage[24] which may lead to diabetes mellitus[16,17].

Creatinine was also significantly raised in HIV/HCV co-infection compared to the HIV, HCV and controls. This is in agreement with previous studies[18, 25]. Creatinine, a product of metabolism is usually excreted from the body through the kidney. The level in the blood rises in renal malfunction and is therefore used as an index of kidney function[18]. Parboosing et. al,[8] had reported cases of renal insufficiency and increased mortality in HCV seropositive South African Cohort of HIV co-infected patients.

Total cholesterol TCH and potassium K+ were incomparable between groups in the study. Our results for AST, ALT, ALP and Creatinine although within normal reference ranges indicated an increasing tendency suggesting the need for early detection and management in other to avert the possibility of hepatic and renal dysfunction in people living with HIV disease co-infected with HCV. This opinion is supported by the reports that HIV modifies the natural history of HCV infection by accelerating the histological progression to end-stage liver disease in a shorter period of time [13, 26, 27]. It is also noteworthy that virological suppressive HIV therapy slows down the pace of HCV disease thereby improving prognosis[28]. Care, however, must be taking in the use of ritonavir because the drug is known to increase the risk of liver injury and elevation of liver enzymes[20, 29, 30].

**Conclusion:** This study revealed rising tendency in the mean values of liver enzymes, Creatinine and RBG among HIV/HCV subjects. The later may increase the non-AIDS-related morbidity and mortality in people living with HIV disease. Rapid detection and management of HCV in our opinion is required in the setting of HIV disease. This we believe will ameliorate complications, such as hepatic and renal dysfunctions, thus reducing the mortality of people living with HIV disease in our environment.

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