



Epidemiological Factors and Liver Enzymes in Patients Co-Infected With HIV/AIDS in a Tertiary Teaching Hospital

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Abstract

Objective: HIV and HCV share routes of infection. Co-infection and its complications are therefore emerging as a major concern as patients on HAART have longer life expectancy. These complications have been well documented. It is necessary to determine in our environment what epidemiological factors are associated. This is expected to improve treatment protocols leading to increase quality of life and prolonged lifespan. Liver enzymes may be useful to monitor therapy. **Materials and Methods:** This is a prospective study. Seventy age and sex matched co-infected patients participated. Sera of the participants were subjected to anti-HCV antibody (IgG) screening using third generation ELISA kit from DIA.PRO, Italy. The epidemiological variables were determined and depicted using bar charts and tables. HIV was determined by detecting the antibodies using two different kits. Determine and Unigold. **Results:** There were 14 males and 56 females in the co-infected group. While there was a definite raise in Liver enzymes in the co-infected patients, only ALT was significantly raised in both sexes and not only the male sex. The majority of patients were above thirty years of age (mean 35.84). Among mono infected and co-infected patients age was the only statistically significant variable. **Conclusion:** It is vital to determine the HCV status of HIV positive patients at any point of entry into a particular health care facility. This would further improve the quality of life and life span of individuals as a result of improved treatment protocols.

Keywords: HIV, HCV, Co-infection, Liver enzymes

INTRODUCTION

Human immunodeficiency virus(HIV) was first discovered by Gallo¹. Hitherto it was described in homosexual men in California and New York in 1981² who presented with Pneumocystis Carinii Pneumonia (PCP).

The prevalence in Africa and especially Nigeria and South Africa have become alarming over time. Sub-Saharan

Africa is more heavily affected by HIV and AIDS than any other region of the world. An estimated 22.9 million people are living with HIV in the region - around two thirds of the global total. In 2010 around 1.2 million people died from AIDS in sub-Saharan Africa and 1.9 million people became infected with HIV. Since the beginning of the epidemic 14.8 million children have lost one or both parents to HIV/AIDS (Yusuf and Benyah,2012).

The social and economic consequences of the AIDS epidemic are widely felt, not only in the health sector but also in education, industry, agriculture, transport, human resources and the economy in general. The AIDS epidemic in sub-Saharan Africa continues to devastate communities, rolling back decades of development progress (Ferreira, et al., 2011).

Hepatitis C virus and HIV co-infection is not uncommon as they share similar routes of infection (Alter,1982; Alter,1989; Garfein, 1996).

This unholy alliance is of particular significance. It has been established that HIV/HCV co-infection can lead to more aggressive liver cirrhosis and carcinoma including hepatic fibrosis and necrosis (Sangiovanni et al; 2004).

Studies have also shown that in treating HIV/HCV co-infection drug-drug interaction could be dangerous (Rodríguez-Torres, 2013) even life threatening (Rodríguez-Torres, 2012).

Treatment against HCV in the co-infected patient is notoriously more complex and challenging. There are no optimal treatment algorithms for HIV/HCV coinfecting patients as efficacy of approved anti-HCV therapies is low with relevant side effects. The use of direct-acting antivirals for anti-HCV therapy has the potential to improve therapeutic efficacy, but also increase side effects and drug-drug interactions. In spite of all of this, the most important and significant fact is that chronic hepatitis C is potentially curable, and the eradication of the HCV infection is a crucial outcome in this population (Rodríguez-Torres, 2013).

Some studies have shown that HIV co-infection has no significant effect on treatment outcomes (Rodríguez-Torres, 2012), however others have described reduced effectiveness when treating HIV co-infection (Braitstein et al, 2004). It should also be mentioned that persistently normal alanine transferase (ALT) levels in this sub population of patients suggests slow HCV disease progression and can be used as a marker.

From the forgoing it is important to monitor liver enzymes as baseline in patients who have been identified as co-infected. This may predict those who will suffer from more severe liver disease or may require treatment modification.

MATERIALS AND METHODS

Study population: Blood samples were collected from 70 consecutive co-infected (HIV/HCV) individuals. These participants were recruited between September 2012 and January 2013 from people living with HIV and AIDS who came to access treatment in our centre and gave informed consent to participate in the study. Ethical clearance was obtained from the Research committee of the Lautech Teaching Hospital research committee (LTH/REC/2013/01/29/127).

Setting: The study was carried out in Osogbo the capital city of Osun state in Nigeria. It is an urban setting with a population of 3,416,959. The residents are majorly Yoruba however there are other tribes including Hausas, Igbos and those of Edo state origin. The weather is typically tropical with periods of heavy rain fall alternating with the dry season.

HIV is usually diagnosed by screening for the antibody using Kits from two different sources Determine and Unigold.

Testing for HCV: About 5mls of blood sample were collected from every participant by venepuncture into EDTA vacutainer bottle (maker: BD, PL6, 7BK, UK Ref. 367836). This was centrifuged at 1200G for 10 minutes and 1ml plasma was harvested into 2 plain bottles for anti –HCV antibody detection with third generation enzyme immunoassay technique.

The plasma from every participant was diluted with DILSPE (sample diluent prepared commercially by DIA.PRO, Sesto San Giovanni, Italy). Each sample was further diluted with DILAS (by DIA.PRO) alongside the negative controls in triplicate, the calibrator in duplicate and a positive control as provided by the kit manufacturer. After the micro plate was incubated and wells washed, all the wells were treated with enzyme conjugate except the first blanking well. The micro plate was incubated again and the chromogen/substrate mixture was added after the second washing.

The reactions were stopped with sulphuric acid and the optical density (OD) was read at 450nm immediately. The cut-off value for the batch was determined and individual results were interpreted as negative (<0.9) and positive (>1.1) and equivocal (0.9-1.1) as appropriate Hepatic Transaminases- This was determined using spectrophotometry. For AST kit with lot number 2549AS and ALT kit with lot 2525AS. Both by Randox, Antrim, United Kingdom.

Statistical analysis: This was done using SPSS software, frequency, mean, standard deviation and t-independent test.
 Inclusion criteria: 1) HIV positive patients 2) HCV positive patients 3) Only patients being managed in our facility.
 Exclusion criteria: 1) HIV negative patients, 2) HCV negative patients 3) Patients not on HAART.

RESULTS

Of the seventy patients 56 (80%) were female and 14 (20%) were male. The majority (71.4%) were above thirty years old. Seventeen (24.3%) had been on HAART for over 40 months. Majority of the participants had primary education 27 (38.6%) while 24 (34.3%) had no education at all. Most of the patients were married 51 (72.9%) while only 5 (7.1%) agreed to having multiple partners. Employment status revealed that 58 (82.9%) of the participants were employed. Of the co-infected patients the only statistically significant variable was age ($p < 0.05$). The others including education, number of partners and employment status were not of statistical significance. In those who were only HIV positive none of these variables were statistically significant. At baseline the patients had been receiving HAART for a mean of $2.10 (\pm 1.6)$ years. None of the patients was on treatment for HCV.

of the co-infected patients analysis of levels of liver enzymes (alanine amino transferase (ALT) and aspartate transaminase (AST)) revealed that ALT was the only enzyme that was of statistical significance ($p > 0.05$) with regards to both male and female sex. Among those who were only HIV positive there was no significance detected.

DISCUSSION

Though it has been suggested that HIV/HCV co infection may have some cardio protective properties (Wheeler et al., 2013) it is generally accepted that the combination is more aggressive (Bourcier et al., 2012; Balogun et al., 2012) especially when drug interactions are taken into consideration when compared with HIV mono-infection. It should also be noted that other viruses maybe present in our patients but have not been tested for including hepatitis Delta and hepatitis E (Victoria et al., 2010) which may individually and together contribute to the pathology. It therefore gives the impression that there is still a lot of research to be carried out especially in our environment on virology in relation to HIV.

In this study the majority of the participants were female (80%) (Table I), this is in contrast to studies carried out in Brazil where most of the patients were male (72.9%) (Victoria et al., 2010). Though it might be mentioned that female patients are more biologically vulnerable to HIV than male patients (Chersich and Rees, 2008) but for co infection male sex is an independent risk factor. Majority of patients were above thirty years old (71.4%) (Bar Chart III). In similar studies most patients were between 25 and 40 years (Victoria et al., 2010; Balogun et al., 2010). In another study it was found that those who were co-infected at a younger age had liver pathology patterns similar to those who had just HIV alone but were ten years older (Kirk et al., 2013) further emphasising the mere aggressive effects of co-infection. Our results did not strictly compare favourably with a study carried out in Brazil which found that co-infection was associated with low income and low educational level (Victoria et al., 2010). (Bar chart IV). This is again reflected in chart II assuming educational status would reflect chances of employment. The contribution of poverty and restricted access to quality healthcare has been highlighted in other similar studies (Klein et al., 2013). Though the study did not reveal any statistical significance with respect to multiple partners it has however been established that having multiple partners is a definite risk factor for co-infection (Bollepalli et al., 2007) majority of patients in our study had just a single partner (Bar chart I). An attempt was made to determine if any the degree and nature of transaminitis in the co-infected patients. It was found that alanine amino transferase (ALT) was statistically ($p < 0.05$) significantly raised in patients who were co-infected compared to those who were not. It had been anticipated that both enzymes would be raised as in other similar studies (Taye and Lakew, 2013). Here both male and female sexes were strongly associated with elevated liver enzymes in contrast to a study carried out in Spain in which only the male sex was strongly associated with liver enzyme elevation (Langohr et al., 2008). It was suggested that the effect of co-infection on sex is lost in co-infected patients making interpretation more complex and inconsistent. It was observed that results of research varied considerably suggesting that environment probably played an important role.

Table 1. Co-infected patients, depicting variables including age, occupation, education and number of partners

	t value	P-Value	Remark
Education	0.281	0.779	N S
No of partners	0.155	0.877	N S
Occupation	0.436	0.664	N S
Age	2.817	0.006	S
Duration On Drugs (Months)	1.871	0.110	N S

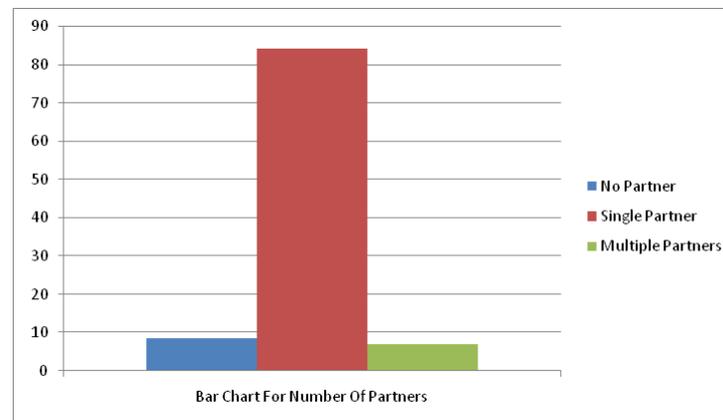
Male=14(20%)
 Female=56(80%)
 Total Patients =70

Table 2. HIV mono infected patients depicting variables including age, occupation, education and number of partners

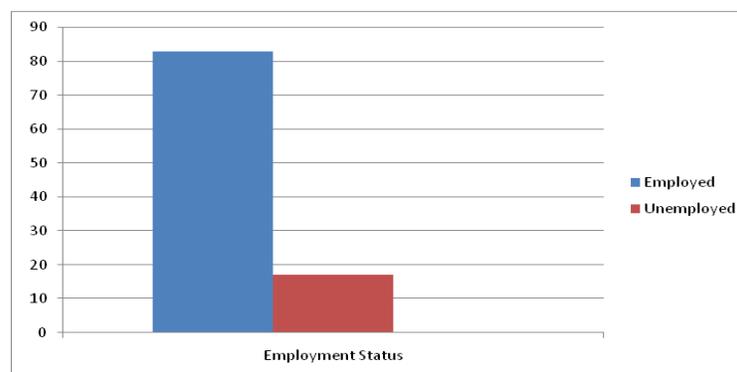
	t value	p-value	Remark
Education	0.443	0.659	N S
No of partners	0.285	0.776	N S
Occupation	0.591	0.557	N S
Age	2.428	0.026	S
Duration on drugs	1.367	0.176	N S

Male=14(20%)
 Female=56(80%)
 Total Patients =70

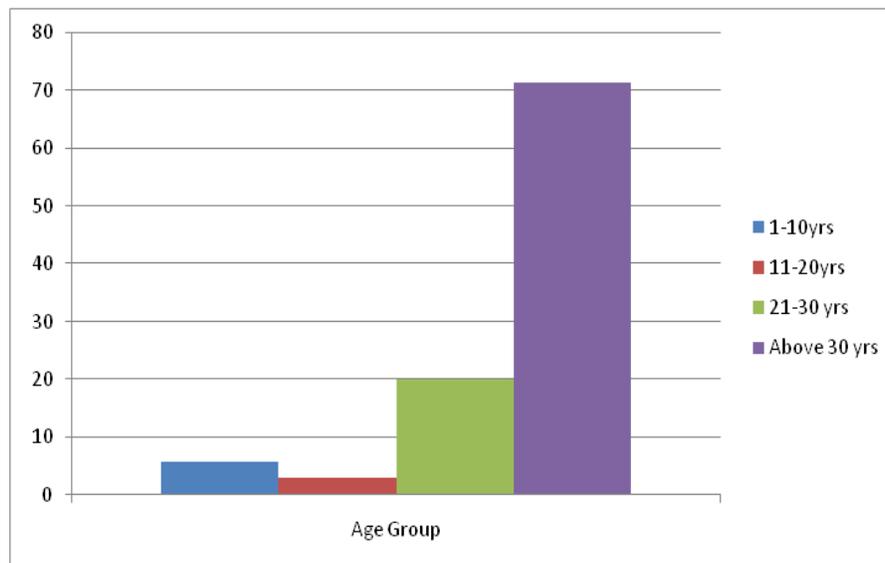
Bar Chart I. Number of partners



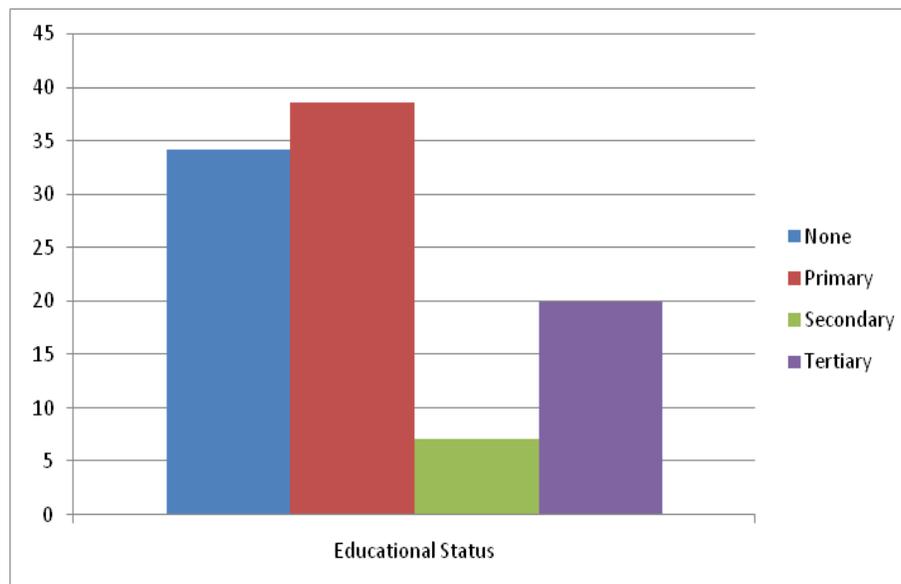
Bar Chart II- Employment Status (co-infected Patients)



Bar Chart III. Age Group



Bar Chart VI. Educational Status



CONCLUSION

HIV and HCV share common routes of infection so the likely hood of them occurring together should not be unexpected. It is important to treat both components of the co-infection adequately. Liver enzymes maybe used to effectively monitor the disease condition especially in resource poor setting such as ours. Further studies would be desired including the AST to platelet ratio index (APRI), a non-invasive marker to determine the extent of liver fibrosis and compare to those that are mono infected.

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References

- Agbaji O, Thio CL, Meloni S, Graham C, Muazu M, Nimzing L, Idoko J, Sankalé JL, Ekong E, Murphy R, Kanki P, Hawkins C. (2013) Impact of hepatitis C virus on HIV response to antiretroviral therapy in Nigeria. *J Acquir Immune Defic Syndr*. Feb 1. 62(2):204-207.
- AIDS Rev. J. 15(1):25-31.
- Alter MJ, Gerety RJ, Smallwood LA, Sampliner RE, Tabor E, Deinhardt F, Frösner G, Matanoski GM (1982). Sporadic non-A, non-B hepatitis, frequency and epidemiology in an urban United States population. *J. Infect. Dis.* 145:886-893.
- Alter MJ, Coleman PJ, Alexander WJ, Kramer E, Miller JK, Mandel E, Hadler SC, Margolis HS (1989). Importance of heterosexual activity in the transmission of hepatitis B and non-A, non-B hepatitis. *JAMA*; 262:1201-1205.
- Balogun TM, Emmanuel S, Ojerinde EF. (2012). HIV, Hepatitis B and C viruses' coinfection among patients in a Nigerian tertiary hospital. *Pan Afr. Med. J.* 12:100.
- Balogun TM, Emmanuel S, Wright KO. (2010) Hepatitis C virus co infection in HIV positive patients. *Nig. Q. J. Hosp Med.* 20(3):117-120.
- Bollepalli S, Mathieson K, Bay C, Hillier A, Post J, Van Thiel DH, Nadir A. (2007). Prevalence of risk factors for hepatitis C virus in HIV-infected and HIV/hepatitis C virus-coinfected patients. *Sex Transm. Dis.* J.34(6):367-370.
- Bourcier V, Winnock M, Ait Ahmed M, Sogni P, Pambrun E, Poizot-Martin I, Chaffaut C, Chevret S, Trinchet JC, Salmon D (2012). Primary liver cancer is more aggressive in HIV-HCV coinfection than in HCV infection. A prospective study. *Clin. Res. Hepatol Gastroenterol. J.* 36(3):214-221
- Braitstein P, Palepu A, Dieterich D, Benhamou Y, Montaner JS. (2004). Special considerations in the initiation and management of antiretroviral therapy in individuals coinfecting with HIV and hepatitis C. *AIDS*. Nov 19; 18(17):2221-2234.
- Chersich MF, Rees HV (2008). Vulnerability of women in southern Africa to infection with HIV: biological determinants and priority health sector interventions. *AIDS . Suppl.* 4:S27-S40.
- De Cock KM, Jaffe HW, Curran JW. (2011) Reflections on 30 years of AIDS. *Emerg Infect Dis. J.* 17(6):1044-1048
- Ferreira PC, Pessôa S, Santos MR (2011). The impact of AIDS on income and human capital. *Econ Inc.* 49(4):1104-1116.
- Fonquernie L, Serfaty L, Charrois A, Wendum D, Lefebvre B, Girard PM, Meynard JL (2004). Significance of hepatitis C virus coinfection with persistently normal alanine aminotransferase levels in HIV-1-infected patients. *HIV Med.* 5(5):385-290.
- Gallo RC, Montagnier L (2003). The discovery of HIV as the cause of AIDS. *N. Engl. J. Med.* 349(24):2283-2285.
- Garfein RS, Vlahov D, Galai N, Doherty MC, Nelson KE (1996). Viral infections in short-term injection drug users: the prevalence of the hepatitis C, hepatitis B, human immunodeficiency, and human T-lymphotropic viruses. *Am. J. Public Health.* 86:655-671.
- Kirk GD, Mehta SH, Astemborski J, Galai N, Washington J, Higgins Y, Balagopal A, Thomas DL (2013). HIV, age, and the severity of hepatitis C virus-related liver disease: a cohort study. *Ann Intern. Med.* 158(9):658-666
- Klein MB, Rollet KC, Saeed S, Cox J, Potter M, Cohen J, Conway B, Cooper C, Côté P, Gill J, Haase D, Haider S, Hull M, Moodie E, Montaner J, Pick N, Rachlis A, Rouleau D, Sandre R, Tyndall M, Walmsley S (2013). HIV and hepatitis C virus co-infection in Canada: challenges and opportunities for reducing preventable morbidity and mortality. *HIV Med.* 14(1):10-20.
- Langohr K, Sanvisens A, Fuster D, Tor J, Serra I, Rey-Joly C, Rivas I, Muga R. (2008). Liver enzyme alterations in HCV-mono infected and HCV/HIV-coinfected patients. *Open AIDS J.* 2:82-88.
- Rodríguez-Torres M (2012). Challenges in the treatment of chronic hepatitis C in the HIV/HCV-coinfected patient. *Expert Rev Anti Infect Ther.* 10(10):1117-1128.
- Rodríguez-Torres M. (2013) Focus on drug interactions: the challenge of treating hepatitis C virus infection with direct-acting antiviral drugs in the HIV-positive patient. *Curr Opin Infect. Dis.* 26(1):50-57.
- Sangiovanni A, Del Ninno E, Fasani P, De Fazio C, Ronchi G, Romeo R, Morabito A, De Franchis R, Colombo M. (2004). Increased survival of cirrhotic patients with a hepatocellular carcinoma detected during surveillance. *Gastroenterology.* 126:1005-1014
- Soriano V, Barreiro P, Sherman KE (2013). The changing epidemiology of liver disease in HIV patients.
- Taye S, Lakew M (2013). Impact of hepatitis C virus co-infection on HIV patients before and after highly active antiretroviral therapy: an immunological and clinical chemistry observation, Addis Ababa, Ethiopia. *BMC Immunol.* 17;14:23.
- Victoria MB, Victoria Fda S, Torres KL, Kashima S, Covas DT, Malheiro A (2010). Epidemiology of HIV/HCV coinfection in patients cared for at the Tropical Medicine Foundation of Amazonas. *Braz. J. Infect. Dis.* 14(2):135-140.
- Wheeler AL, Scherzer R, Lee D, Delaney JA, Bacchetti P, Shlipak MG, Sidney S, Grunfeld C, Tien PC; (2013) HIV/HCV coinfection ameliorates the atherogenic lipoprotein abnormalities of HIV infection. *AIDS*. Oct 16 [Epub ahead of print]
- Yusuf TT, Benyah F (2012). Optimal strategy for controlling the spread of HIV/AIDS disease: a case study of South. *Afr. J. Biol. Dyn.* 6(2):475-494.