ORIGINAL ARTICLE

Hepatic transaminase and alkaline phosphatase enzyme levels in HIV/HBV co-infected and HIV mono-infected patients in Maiduguri, Nigeria

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Abstract

Background: Studies have shown that HIV-HBV co-infected patients have an increased risk of liver-related morbidity and mortality compared to their HIV-mono-infected counterparts. Furthermore, it has been reported that HIV-HBV co-infected patients have a significantly high incidence of drug-induced hepatotoxicity following commencement of HAART than HIV-mono-infected patients.

Objectives: To compare the levels of aspartate amino transferase (AST), alanine amino transferase (ALT) and alkaline phosphatase ($ALKPO_4$) enzyme levels between HAART naïve HIV-HBV co-infected patients and their HIV-mono-infected counterparts.

Materials and Methods: A cross-sectional descriptive study in which 142 newly diagnosed HIV/HBV co-infected and HIV mono-infected adults were investigated for alkaline aminotransferase, aspartate aminotransferase and alkaline phosphatase enzyme levels.

Results: The study subjects comprised of 80 (56.3%) females and 62 (46.7%) males. The age range of the study population was 15-65 years. The mean ages of male and female subjects were 45.5 ± 10.5 years and 39.1 ± 7.5 years respectively ($P < 0.05$). Sixty-three (44.4%) study subjects were HIV/HBV co-infected while 79 (55.6%) were HIV mono-infected. The mean ALT enzyme level of HIV/HBV co-infected subjects was significantly higher than that of HIV mono-infected ones i.e., 42.12 IU/l vs. 27.86 IU/l, ($P = 0.038$). However, there was no statistically significant difference in the mean AST (30.14 IU/l vs. 29.09 IU/l, $P = 0.893$) and $ALKPO_4$ (55.86 IU/l vs. 60.97 IU/l, $P = 0.205$) enzyme levels between HIV-HBV co-infected and HIV mono-infected subjects albeit the two enzymes were moderately elevated in both categories of subjects.

Conclusion: The significantly elevated ALT enzyme levels amongst HIV-HBV co-infected subjects suggest that HIV-HBV co-infected patients may have an increased risk of liver-related morbidity and mortality than their HIV mono-infected counterparts. Screening for serological markers of chronic HBV infection, as well as hepatic transaminase enzyme levels in all newly diagnosed HIV-positive patients is therefore recommended before commencement of HAART.

Key words: Alkaline phosphatase enzyme, hepatitis B virus surface antigen, hepatic transaminase enzymes, human immunodeficiency virus

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Introduction

Areas of the world with the highest hepatitis B virus (HBV) endemicity including Nigeria correspond to areas with the highest incidence of human immunodeficiency virus (HIV) infection.[1-5] Human immunodeficiency virus and HBV co-infection have been a growing global health

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problem, especially in underprivileged and underdeveloped sub-Saharan African countries. Nigeria is highly endemic for HBV with a chronic HBV prevalence rate of 11-21% in blood donors and 11-15% in HIV-infected persons.[2-5] Although, the advent of highly active antiretroviral therapy (HAART) has reduced mortality in the HIV-infected population, it has consequently led to an increase in the prevalence of chronic co-infections such as with HBV.[7] According to recent research, the rate of HBV co-infection in HIV-positive patients is increasing.[2,6,7]

Hepatitis B virus has little impact on HIV disease progression; however, HIV renders HBV more aggressive in co-infected individuals.[6] Studies have shown that HIV-HBV co-infected patients are 19 times more likely to die of liver-related mortality than their HIV-monoinfected counterparts.[7,8] Human immunodeficiency virus and HBV co-infection increases hepatotoxicity from highly active antiretroviral therapy (HAART) by three to four folds, and the risk may be even greater in those with a higher CD4+ cell count change indicating a role for immune reconstitution. Some studies have also demonstrated decreased response to HAART in the setting of chronic HBV coinfection.[7,8] This problem is further compounded in developing countries like ours by lack of proper funding of research programs on HIV-HBV co-infection, inadequate diagnostic facilities for detecting concurrent diseases in HIV-infected patients (e.g., HBV), lack of facilities for detecting early HAART-related hepatotoxicity, and lack of effective HBV treatment; all of which could have a great impact on the effective management of this affected population. In Nigeria, only a few centers carry out routine screening for HBsAg in HIV-positive patients, as it is not yet adopted as a national policy by the government. This lapse may continue to expose a lot of HIV-HBV co-infected patients to HAART-related hepatotoxicity and other HBV associated hepatic disorders.[2,8,9]

With the increasing number of patients accessing HAART in Nigeria, HBV coinfection will continue to be a growing health concern among HIV-positive population in the few decades to come unless and until our government implements a national guideline for the control, as well as management of this potential health threat among HIV-infected persons.

Aim of the study

To compare hepatic transaminase and alkaline phosphatase enzymes levels between HAART naïve HIV/HBV co-infected and HIV mono-infected patients.

Materials and Methods

Study area

The study was carried out at the University of Maiduguri Teaching Hospital, North Eastern Nigeria.

Study design

The study was a cross-sectional descriptive study.

Study population

The study subjects were newly diagnosed HIV-positive adults ≥14 years of age. The study subject were selected by systematic random sampling method i.e., every third HIV-positive patient referred to the ART clinic who fulfilled the entry criteria was recruited in to the study.

Inclusion criteria

- Newly diagnosed HIV-infected patients ≥14 years of age
- Consenting patients.

Exclusion criteria

- Non consent
- Patients younger than 14 years of age
- Patients with other causes of chronic liver disease other than HBV
- Patients who had tested positive for anti-HCV antibody
- HIV-negative patients
- HAART experienced HIV-positive patients
- HIV-TB co-infected patients.

Sample size

Based on HIV prevalence of 3.2% in Borno state, Epi Info statistical software was used to calculate the sample size, an α-level of 5% and 1-β of 80% were used.

Materials and test Methods

On entry into the study, a detailed history was obtained and full clinical examination was carried out followed by administration of a structured questionnaire to each patient, giving detailed demographic, clinical and laboratory data.

Five milliliters of blood sample was collected from each subject by venepuncture after cleansing site with methylated spirit. This was placed in plain tubes and allowed to clot. The sera were separated from the cells, frozen at −20°C to be tested within 72 h. Blood levels of alanine amino transaminase, aspartate amino transaminase and alkaline phosphatase enzyme levels were subsequently determined using an auto-analyser. Five milliliters of blood sample was collected from each subject by venepuncture after cleansing site with methylated spirit. This was placed in plain tubes and allowed to clot. The serum was separated from the cells, frozen at −20°C to be tested within 72 h. Blood levels of alanine amino transaminase, aspartate amino transaminase and alkaline phosphatase enzyme levels were subsequently determined using automatic analyzer (automatic serum analyser, RMD Mediaids, PVT Ltd, 301-302, Magnum House, New Delhi-11015, India).

Human immunodeficiency virus (HIV) screening test was done by the UNIGOLD and DETERMINE rapid test methods (UNIGOLD™ Recombigen®/DETERMINE™ rapid test, Trinity Biotech, Jamestown NY, USA); positive cases were subsequently confirmed by the western blotting method method (QualiCode™, Immunetics, Inc, 27 Drydock Avenue, 6th floor, Boston, MA, 02210-2377, USA). Hepatitis B surface antigen (HBsAg) test was done using the ELISA test method (ELISA, CALTECH, C.A, USA).

Ethical consideration

Ethical approval for the study was obtained from the Ethical Committee of the University of Maiduguri Teaching Hospital. A signed or thumb-printed informed consent was obtained from the patients before commencing the study. Patients were at liberty to deny consent for or opt out of the study at any stage without any consequences.

Results

One hundred and forty-two newly diagnosed HIV positive subjects were recruited into the study. Out of these 80 (56.3%) were females and 62 (43.7%) males. Their ages ranged between 15 and 65 years. The mean ages for male and female subjects were 45.5 ± 10.5 years and 39.1 ± 7.5 years, respectively, ($P < 0.05$). Sixty-three (44.4%) subjects were HBsAg positive and the remaining 79 (55.6%) were HBsAg negative [Table 1].

The distribution of alanine amino transferase (ALT) enzyme levels between HBsAg positive and HBsAg negative subjects is shown in Table 2. The mean ALT level of HBsAg positive patients was 42.12 IU/l and that of HBsAg negative patients was 27.86 IU/l, ($P = 0.036$). Moreover, scores of the study subjects (i.e. 31.65%) who had serum ALT enzyme levels within normal limits were found amongst HBsAg negative individuals, ($P = 0.013$). Conversely, HBsAg positive subjects constituted quite a substantial proportion (28.57%) of individuals with ALT enzyme levels greater than 5 times the upper limit of normal (i.e. >60 IU/l), ($P = 0.030$).

Table 3 compared the distribution of aspartate amino transferase (AST) enzyme levels between HBsAg positive and HBsAg negative subjects. The mean AST level of HBsAg positive subjects was 30.14 IU/l and that of negative ones was 29.09 IU/l. There was no statistically significant difference between the two means ($P = 0.893$). However, HBsAg positive subjects constituted a statistically significant proportion (i.e. 33.33%) amongst individuals with moderately elevated levels of AST enzyme (i.e. 25-36 IU/l), ($P = 0.025$).

Table 4 compared alkaline phosphatase ($AlkPO_4$) enzyme levels between HBsAg positive and negative subjects of the study population. The mean $AlkPO_4$ enzyme level of HBsAg positive subjects was 55.86 IU/l while that of their HBsAg negative counterparts was 60.97 IU/l. There was no statistically significant difference between the means of the two groups ($P = 0.205$).

Furthermore, HIV/HBV co-infected patients have a significantly lower mean CD4+ cell counts and higher mean ALT enzyme levels compared to their HIV-monoinfected counterparts [Table 5].

Table 1: Age and sex distribution of the study population

Age group (years)	Sex		
	Female *N* (%)	Male *N* (%)	*P* value
15-19	0 (0.00)	1 (1.70)	0.402
20-24	1 (1.25)	9 (13.56)	0.014*
25-29	13 (17.07)	16 (25.42)	0.321
30-34	13 (17.07)	17 (27.12)	0.240
35-39	21 (26.83)	11 (18.64)	0.331
40-44	8 (9.76)	3 (5.08)	0.368
45-49	8 (9.76)	4 (6.78)	0.589
50-54	2 (2.44)	0 (0.00)	0.228
55-59	12 (14.63)	1 (1.70)	0.013*
≥60	2 (2.44)	0 (0.00)	0.228

*Statistically significant

Table 2: Distribution of alanine amino transferase enzyme levels and HBsAg status of the study population

ALT levels (IU/L)	HBsAg status		*P* value
	Positive *N* (%)	Negative *N* (%)	
0-12	3 (4.76)	25 (31.65)	0.013*
13-24	21 (33.33)	28 (35.44)	0.857
25-36	12 (19.05)	8 (10.13)	0.263
37-48	9 (14.29)	6 (7.59)	0.341
49-60	0 (0.00)	4 (5.06)	0.293
>60	18 (28.57)	8 (10.13)	0.030*
Total *N* (%)	63 (100)	79 (100)	

*Statistically significant; HBsAg=Hepatitis B surface antigen; ALT=Alanine amino transferase

Table 3: Distribution of aspartate amino transferase enzyme levels and HBsAg status of the study population

AST levels (IU/L)	HBsAg status		*P* value
	Positive *N* (%)	Negative *N* (%)	
0-12	18 (28.57)	26 (32.91)	0.705
13-24	18 (28.57)	25 (31.65)	0.787
25-36	21 (33.33)	10 (12.66)	0.025*
37-48	0 (0.00)	4 (5.06)	0.293
49-60	0 (0.00)	4 (5.06)	0.293
>60	6 (9.53)	10 (12.66)	0.694
Total *N* (%)	63 (100)	79 (100)	

*Statistically significant; HBsAg=Hepatitis B surface antigen; AST=Aspartate amino transferase

Discussion

The scourge of the HIV/AIDS pandemic is most felt in sub-Saharan Africa where it has been estimated that about 9% of its adult population are living with the virus.[10] Nigeria, being the most populous country on the African continent will continue to remain vulnerable to the threats of HIV/AIDS and other chronic viral infections including HBV.[11] There is evidence that co-infection with HBV will contribute significantly to morbidity and mortality within the HIV positive population over the coming years; this may be partly due to increase in survival of HIV-infected patients as a result of accessibility to highly active antiretroviral therapy (HAART) in developing countries.[2] Studies have shown that HBV co-infection in the setting of HIV complicates the clinical course and management of HIV infection.[2] It may also adversely affect therapy for HIV infection. The reported co-infection rates of HIV and HBV have been variable worldwide depending on the geographic region, risk groups and the type of exposure involved.[3] Within Nigeria, various prevalence rates of HIV and HBV co-infections have been reported from region to region.

The mean serum alanine amino transferase (ALT) enzyme level of HIV-HBV co-infected subjects was significantly higher than those of HIV mono infected subjects in this study. It was also observed in the study that HIV-HBV co-infected subjects constituted quite a sizable proportion of persons with ALT enzyme levels greater than 5 times the upper limit of normal (ALT normal range for study area/center: 1-22 IU/l). This may lend credence to the fact that HIV-HBV co-infected patients have an increased risk of liver related morbidity and mortality than their HIV mono infected counterparts.[3] Although a comparison of the mean aspartate amino transferase (AST) enzyme level between HIV-HBV co-infected and HIV mono-infected subjects in the study did not reveal any statistically significant disparity between the two groups, however HIV-HBV co-infected subjects constituted a statistically significant majority amongst individuals with moderate elevation of AST enzyme levels (AST normal limit for study area/center: 1-15 IU/l). These findings were similar to those reported by Otedo *et al.*,[12] in Kenya; mean ALT 375 (±213) IU/l for HIV-HBV co-infected subjects vs. 338 (±135) IU/l for HIV mono-infected subjects ($P = 0.05$) and mean AST 286 (±117) IU/l for HIV-HBV co-infected subjects compared with 306 (±175) IU/l for HIV mono-infected subjects ($P = 0.230$). On the contrary, other workers like Rai *et al.*,[13] in India have demonstrated a significant rise in the mean levels of both transaminase enzymes in co-infected subjects compared with HIV mono-infected ones. Conversely, Shazia and colleagues[14] working in Mumbai, India, did not find a significant rise in the transminase enzyme levels amongst both HIV-HBV co-infected and HIV mono-infected subjects. Since serum ALT enzyme is more specific to the liver, its increase either in isolation or together with AST may suggest an active HBV disease. The variation in the transaminase enzyme levels in the various studies could also reflect the difference in socio-demographic, as well as clinical characteristics of the study populations involved.[3]

Table 4: Distribution of alkaline phosphatase ($ALKPO_4$) enzyme levels and HBsAg status of the study population

$ALKPO_4$ (IU/L)	HBsAg status		*P* value
	Positive *N* (%)	Negative *N* (%)	
0-35	27 (42.86)	23 (29.11)	0.230
36-70	21 (33.33)	24 (30.38)	0.795
71-105	9 (14.29)	22 (27.85)	0.202
>105	6 (9.52)	10 (12.66)	0.694
Total *N* (%)	63 (100)	79 (100)	

HBsAg=Hepatitis B surface antigen

Table 5: Relationship of the mean CD4 cells count and the mean enzyme levels between HIV/HBV co-infected and HIV-monoinfected patients

	HIV-HBV	HIV	*P* value
Mean CD4+ cell count (cells/μl)	105.43	161.35	0.038*
Mean ALT (IU/l)	42.12	27.86	0.049*
Mean AST (IU/l)	30.14	29.09	0.893
Mean $ALPO_4$ (IU/l)	55.86	60.97	0.205

*Statistically significant; $ALPO_4$=Alkaline phosphatase; HIV=Human immunodeficiency virus; HBV=Hepatitis B virus

In a similar vein, it has been observed that there was no statistically significant difference between the mean serum levels of alkaline phosphatase ($AlkPO_4$) enzyme of HIV-HBV co-infected subjects and those of HIV mono-infected ones, although the levels were raised in both categories of patients ($AlkPO_4$ normal limit for study area/center: 60-170 IU/l). This enzyme is also non-specific to the liver as its level can increase in other disease states e.g., HIV infection, bone diseases, chronic renal disease etc. This finding is also in concordance with those reported by other workers, for example Otedo *et al.*,[12] in Kenya observed that HIV/AIDS patients were more prone to various multi-systemic inflammatory conditions due to dysfunction in both qualitative and quantitative cellular immunity thereby resulting in the elevation of hepatic transaminases, as well as alkaline phosphatase enzyme levels.

Conclusion

The finding of a statistically significant mean serum ALT enzyme level among HIV-HBV co-infected subjects, as well as moderate elevation of AST enzyme level between these two sub-populations (i.e. HIV-HBV co-infected and HIV mono-infected subjects) further corroborate the fact that HIV-HBV co-infected persons may be more prone to

liver related complications than their HIV mono infected counterparts, and this calls for an intervention. From the foregoing, it is pertinent therefore to consider screening all HIV infected persons for markers of chronic HBV infection, as clinical assessment alone may be unhelpful in identifying potentially co-infected persons.

References

1. Mahoney FJ. Update on the diagnosis, management and prevention of hepatitis B virus infection. Clin Microbiol Rev 1999;12:351-66.
2. Bojuwoye BJ. The burden viral hepatitis in Africa. West Afr J Med 1997;16:198-203.
3. Burnett RJ, Francois G, Kew MC, Leroux-Roels G, Meheus A, Hoosen AA, *et al*. Hepatitis B virus and human immunodeficiency virus co-infection in sub-Saharan Africa: A call for further investigation. Liver Int 2005;2:201-13.
4. Otegbayo JA, Fasola FA, Abja A. Prevalence of hepatitis B surface and "e" antigens, risk factors for viral acquisition and serum transaminase among blood donors in Ibadan, Nigeria. Trop Gastroenterol 2003;24:196-7.
5. Oronsaye FE, Oronsaye JI. Prevalence of HIV positives and hepatitis B surface antigen positives among blood donors in the University of Benin Teaching Hospital, Nigeria. Trop Doct 2004;34:156-60.
6. Thio CL, Seaberg EC, Skolasky R Jr, Phair J, Visscher B, Muñoz A, *et al*. HIV-1, hepatitis B virus and risk of liver related mortality in the multi centre AIDS cohort study (MACS). Lancet 2002;360:1921-6.
7. Saves M, Vandentorren S, Dancourt V, Marimoutou C, Dupon M, Couzigou P, *et al*. Severe hepatic cytolysis: Incidence and risk factors in patients treated by antiretroviral combinations. Acquitane cohort, France, 1996-1998. AIDS 1999;13:115-21.
8. Sheng WH, Chen MY, Hsieh SM, Hsiao CF, Wang JT, Hung CC, *et al*. Impact of hepatitis B virus infection on the outcome of patients infected with HIV in an area where HBV infection is hyperendemic. Clin Infect Dis 2004;38:147-8.
9. Rodriguez-Rosado R, Garcia-Samaniego J, Soriano V. Hepatotoxicity after introduction of highly active antiretroviral therapy. AIDS 1998;12:1256.
10. AIDS Epidemic Update. Joint United Nations Programme on HIV/AIDS (UNAIDS) and World Health Organisation (WHO) Bulletin, Geneva 2007:2:102-12.
11. National HIV Seroprevalence Sentinel Survey; 2005. Nigeria Federal Ministry of Health (FMOH) Technical Report 2006. p. 12-7.
12. Otedo AE. Hepatitis B virus and HBV coinfection at Kisumu Distric Hospital, Kenya. East Afr Med J 2004.8;12:626-30.
13. Rai RR, Mathur A, Mathur D, Udawat HP, Nepalia S, Nijhawan S, *et al*. Prevalence of occult hepatitis B and C in HIV patients infected through sexual transmission. Trop Gastroenterol 2007;28:19-23.
14. Shazia MA, Mehta PR. Human immunodeficiency virus, HBV, HCV coinfection. Bombay Hospital Journal 2001;6:196-7.

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