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LIVER FUNCTION TESTS IN HIV-1 INFECTED ASYMPTOMATIC PATIENTS AND HIV-1 AIDS PATIENTS WITHOUT HEPATOMEGALY IN LAGOS, NIGERIA

[1]Ogunro, P. S., [1]Oparinde, D. P., [2]Okesina, A. B.

Department of [1]Chemical Pathology/Immunology,
College of Health Sciences, Ladoke Akintola University of Technology
PMB 4400, Osogbo, Nigeria
Department of [2]Chemical Pathology/Immunology,
College of Medicine, University of Ilorin, Ilorin, Nigeria

Correspondence to: Dr. P. S. Ogunro (E-mail:- ogunrops@yahoo.com)

Hepatic functions were assessed by serum assays of albumin (ALB), total protein (TP), total bilirubin (TB), conjugated bilirubin (CB), serum activities of alanine transaminase (ALT), aspartate transaminase (AST), alkaline phosphatase (ALP) and gamma – glutamyl transferase (GGT) in 51 HIV-1AIDS patients, 38 HIV-1 infected asymptomatic patients and 56 age and sex matched healthy HIV negative controls. The mean ± SEM serum ALB concentration of 23.5 ± 1.2 g/L in AIDS patients was significantly lower ($p < 0.001$) than those of HIV-1 infected asymptomatic patients and healthy controls; 38.9 ± 3.1g/L and 39.4 ± 2.8g/L respectively. The mean ± SEM TB concentration of 17.8 ± 1.3 µmol/L in AIDS patients was significantly higher ($p < 0.01$) than 11.7 ± 1.1µmol/L observed in HIV-1 infected asymptomatic patients and 10.8 ± 2.1µmol/L in the controls. Similarly, there was a significant elevation ($p < 0.05$) in serum CB concentration of 6.5 ± 0.9µmol/L in AIDS patients compared to HIV-I infected patients of 3.8 ± 1.0 µmol/L and controls of 3.1 ± 0.8 µmol/L. The mean ± SEM ALT, AST, ALP and GGT activities (iu/L) of 48.7 ± 3.1, 54.3 ± 3.3, 84.8 ± 4.3 and 47.5 ± 4.1 respectively in AIDS patients were significantly higher ($p < 0.001$) than 21.3 ± 2.9, 25.6 ± 1.3, 56.4 ± 3.2 and 25.1 ± 1.7 respectively observed for the same enzymes in HIV-1 infected patients and 20.1 ± 3.1, 24.5 ± 2.6, 54.6 ± 4.3 and 24.2 ± 2.1 respectively in the controls. These results provide evidence to suggest that hepatic damage is greater in AIDS patients than in HIV-1 infected asymptomatic patients even in the absence of hepatomegaly. We conclude that this may be due to opportunistic infections that set in at the later part of HIV-1 infection (i.e. at AIDS stage) or increase severity of HIV-1 infection or both

Key Words: HIV-1 infected asymptomatic patient, AIDS, Hepatic functions

INTRODUCTION

Patients infected with Human Immunodeficiency Virus (HIV), the causative agent of Acquired Immunodeficiency Syndrome (AIDS), display a broad spectrum of clinical manifestations ranging from asymptomatic state to life threatening symptomatic state characterized by opportunistic infections and malignancies (1).

The hallmark of HIV infection is the cytopathic effect on the CD4 bearing cells (Helper T4 cells) (2). Apart from these cells, other CD4 protein bearing cells such as macrophages, B-lymphocyte, microglial cells, haemopoietic stem cells, rectal mucosal cells, Kupffer cells and liver sinusoid epithelial cells are also affected (3) HIV is a pathogen that causes a variety of specific and non-specific defects in immune function that result in diverse clinical consequences. Studies in the USA and Europe (4) indicate that approximately 50% of HIV infected patients will develop AIDS by 10 years; 75% by 15 years and 90% by 20 years (4).

In about two weeks after infection with HIV, approximately 50% of patients will develop a viral illness that may resemble glandular fever, influenza or aseptic meningitis. In more severe cases,

hepatomegaly and raised transaminases may be detected (5, 6).

Hepatomegaly is a frequent finding in about two-third of AIDS patients and some abnormalities in liver function tests of HIV and AIDS patients have been reported (7, 8). The cause of this hepatomegaly has been ascribed to various mechanisms such as infection arising from HIV, hepatitis B, non-A non-B, sepsis, alcoholic liver disease and malnutrition (8-14). Although the presence of hepatomegaly indicates some degree of hepatocellular damage and or hepatobiliary obstruction in HIV-1 AIDS patients, it is not however clear whether hepatic pathology exists in HIV-1 infected asymptomatic and HIV-1 AIDS patients without hepatomegaly.

This study compares the biochemical indices of liver cell damage and hepatobiliary obstruction in HIV-1 infected asymptomatic and HIV-1 AIDS patients without hepatomegaly.

MATERIALS AND METHOD

The study was carried out after obtaining approval from the Ethical Committee of the Lagos University Teaching Hospital, Nigeria. Forty five AIDS patients and 38 HIV-1 infected patients were randomly selected from those seen in LUTH for this study. The HIV-1 infected asymptomatic patients consists 16 males and 22 females aged between 20-70 years from among those found seropositive by ELISA method (15) and confirmed by Western Blot (16). The full-blown HIV-I AIDS patients consist 19 males and 26 females aged between 20-70 years. Fifty six control subjects, 25 males and 31 females, were selected from healthy individuals matched for age and sex who were screened and found negative for HIV-I and II.

Subjects who had evidence of hepatitis B, non-A non-B, alcoholic liver disease, hepatomegaly, sepsis, malnutrition and those on cytotoxic drugs were excluded from the study. Screening for hepatitis was carried on each subject and control, using Wellcome ELISA kit. Those positive were excluded from the study.

About 5 milliliters of venous blood was collected from each of the subject and control and was allowed to clot and retract. Serum was obtained after centrifugation at 3,500 rpm for 10 minutes and the samples were stored frozen at – 20°C until analyzed. Lyophilized controls were obtained from Randox Laboratory. Analysis was carried out in batches with the aid of BECKMAN SYNCHRON (CX5 serial no 4562) autoanalyser, using appropriate control with each batch. Serum albumin was estimated based on the dye-binding method of Doumas, Watson and Biggs (17), total protein by the method of Doumas, Bayse and Carter (18), total and conjugated bilirubin by the method of Malloy and Evelyn (19), AST by the method of Karmen (20), ALT by the method of Wroblewski and LaDue (21), ALP by the method of Bassey *et al* (22) and GGT by the method recommended by IFCC Part 4 (23). Results obtained were subjected to statistical analysis using computer with EPI-INFO version 6.2 software. The Student's t-test was used to determine the differences between the means of the various groups.

RESULTS

Table 1 displayed the demographic characteristics of sample population while Table 2 displayed the summarized comparative mean ± SEM of hepatic biochemical parameters in the two groups of

subjects and the controls. The result shows a significant decrease ($p < 0.001$) in the mean serum concentration of albumin in AIDS patients when compared with healthy controls and HIV-1 infected asymptomatic patients. Also, a significant increase ($p < 0.0I$) in serum level of total bilirubin was observed in AIDS patients compared to HIV-1 infected patients and healthy controls. Similarly, there was a significant elevation ($p < 0.05$) in the serum level of conjugated bilirubin in AIDS patients when compared to HIV-1 infected asymptomatic patients and the controls.

The mean serum activities of ALT and AST in AIDS patients were significantly increased ($P<0.001$) when compared with those of HIV-1 infected asymptomatic patients and the controls. The ALT and AST activities in the controls were not significantly different from those of the HIV-1 infected asymptomatic individuals. The mean serum activities of ALP and GGT in AIDS patients were significantly increased ($P<0.001$) when compared with those of HIV-1 infected asymptomatic patients and controls respectively. The mean serum activities of ALP and GGT in controls were not significantly different from those of HIV-1 infected asymptomatic individuals.

Table 1: Demographic characteristics of sample population

Age group (In years)	Control		HIV- 1 infected		AIDS	
	Male	Female	Male	Female	Male	Female
20 - 40	12	15	9	10	10	14
41 - 60	9	12	5	8	8	10
> 60	4	4	2	4	1	2

Table 2: Means ± SEM of hepatic biochemical parameters in HIV-1 infected Patients and AIDS patients without hepatomegaly, and controls

Parameter/Unit	Control	HIV-1 infected	AIDS		
Albumin (g/L)	39.4 ± 2.8	38.9±3.1	23.5±1.2	♦♦♦	***
Total Protein(g/L)	74.3 ± 5.1	73.6±6.3	72.9±4.8		
Bil. Total(µmol/L)	10.8 ± 2.1	11.7±1.1	17.8±1.3	♦♦	**
Bil. Conj(µmol/L)	3.1 ± 0.8	3.8±1.0	6.5±0.9	♦	*
ALT (IU/L)	20.6±3.1	21.3±2.9	48.7±3.1	♦♦♦	***
AST (IU/L)	24.5±2.6	25.6±1.3	54.3±3.3	♦♦♦	***
ALP (IU/L)	54.6±4.3	56.4±3.2	84.8±4.3	♦♦♦	***
GGT (IU/L)	24.2±2.1	25.1±1.7	47.5±4.1	♦♦♦	***
Alb./Globulin Ratio	39.4/34.9	38.9/34.7	23.5/49.4	♦♦	**

♦= P < 0.05; ♦♦= P < 0.01 and ♦♦♦ = P < 0.001------AIDS Vs Controls
*= P < 0.05, ** = P < 0.01 and *** = P < 0.001------AIDS Vs HIV-1 infected

DISCUSSION

In this study, the concentration of serum albumin was found to be low in AIDS patients compared to controls. This finding is similar to the study of Geffriand *et al* (24), who found that serum albumin was

significantly reduced in AIDS patients. But Cello (25) and Cappell (26) reported no significant reduction in albumin concentration when AIDS patients were compared with controls. In acute liver disease, there may be little or no reduction in plasma albumin because its biological half-life is about 20 days and also the fractional clearance rate is very low (27). Apart from chronic hepatic lesions, hypoalbuminaemia found in this group of patients, may be due to increased catabolism from tissue damage, inflammation, malnutrition, malabsorption syndromes and protein loss (28). It has been observed that majority of patients with AIDS who develop diarrhoea have some degree of malabsorption (29). All the AIDS patients in our study had diarrhoea and this may have synergistically contributed to hypoalbuminaemia resulting from reduced synthetic liver function.

The observed significant reduction in the mean ± SEM plasma albumin in AIDS patients compared to the control subjects suggests a chronic hepatic dysfunction. This is further corroborated by the significant elevation of the mean ± SEM plasma activities of ALT and AST in AIDS patients compared to the controls and HIV-1 infected asymptomatic group. This observation is in keeping with the works of other researchers (7, 25, 26, 30), who found similarly elevated ALT and AST in AIDS patients compared with controls.

The total protein found in both HIV-1 and AIDS patients does not differ from that of the control, but there is a reversal of albumin/globulin ratio in AIDS patients with a higher globulin fraction. A similar pattern has been reported by Mohammed (31) who noticed that AIDS patients have persistent generalized lymphadenopathy with hyperplasia of the B-lymphocytes in lymphoid follicles and polyclonal hypergammaglobulinopathy involving IgG, IgA and rarely IgM. Similar pattern of hypergammaglobulinaemia has been confirmed in AIDS patients in Northern Nigeria (32).

Our study showed a significantly elevated serum total bilirubin and conjugated bilirubin, which may indicate problem with excretory function of the liver. Though the subjects were not clinically jaundiced, this may be a pointer to hepatic pathology involving hepatocytes and its enzymes or an increase in the rate of haemolysis or a decreased rate of delivery of unconjugated bilirubin to the liver secondary to hypoalbuminaemia in this group of subjects.

Our observation tallies with the work of Dworkin *et al* (33) who found that significant rises in serum ALP and total bilirubin occurs during the course of AIDS in American patients. However Astagueau *et al* (34) in France, Cello *et al* (25) and Cappell *et al* (26) in America, reported that jaundice was rare in AIDS patients. Serum transaminases ALT and AST activities were significantly raised in AIDS patients compared to those of the healthy individuals, this is suggestive of an increased degree of hepatocellular damage in AIDS patients. This observation has been noted in previous studies carried out on American whites and blacks (12, 25, 26, 30), and by some other workers (24, 35, 36) who also found raised serum activities of ALT and AST in AIDS patients compared to healthy individuals. Opportunistic infections

of the liver such as *Mycobacterium avium-intracellulare*, *Mycobacterium tuberculosis*, Cytomegalovirus, *Cryptococcus neoformans*, and *Pneumocystis carinii* which are common complications in AIDS patients have been implicated as the cause of liver parenchymal cell damage (25).

Significantly elevated serum ALP and GGT observed in AIDS patients may be a pointer to a higher degree of damage that results in hepatobiliary obstruction in this group of subjects. Invasive and non-invasive diagnostic procedures have revealed and documented papillary stenosis, sclerosing cholangitis, cholecystitis as well as thickened gall bladder wall in a growing population of AIDS patients (14). All these structural abnormalities have been attributed to opportunistic infections. Our findings agree with the previous studies in America (13, 14, 25, 26, 30, 37), and some other parts of the world where a similarly elevated ALP and GGT in AIDS patients was found (35, 36, 38). Previous studies explained that this biochemical relationship is compatible with localized biliary obstructive lesions in liver due to localized CD4 site in the liver sinusoid epithelial cell surfaces (39, 40, 41).

Opportunistic infections in late stage of the disease (AIDS) may likely be the cause of hepatic damage in this study however the time of onset or degree of infection was not determined to establish whether difference in findings between asymptomatic HIV-1 infected and AIDS patients are due to severity of the condition. This possibility cannot be totally ruled out.

CONCLUSION

The significant reduction in the serum albumin is a strong pointer to the presence of chronic hepatic lesion in patients with AIDS although various other possibilities like diarrhoea were adduced in the discussion. Our result shows that hepatic lesion in AIDS patients without hepatomegaly affects both hepatocellular integrity and hepatobiliary obstruction with a greater severity than HIV-1 infected asymptomatic patients without hepatomegaly. We therefore conclude that the level of hepatic function distortion is greater in AIDS patients than in HIV-1 infected asymptomatic patients even in the absence of hepatomegaly. Further work need to be carried out to determine whether the level of distortion of hepatic function is similar in these two groups of patients in the presence of hepatomegaly.

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