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Changes in lipid profile and liver enzymes in HIV infection and AIDS Patients

Mahendra R. Pakhale, Dr. Trupti Ramteke, Dr. Arun Tadas

Dept. of Biochemistry S.V.N.Govt. Medical College, Yavatmal (MS) India

Abstract- This study was designed to find the correlation between changes in lipid profile and liver marker enzymes in HIV-infected and AIDS patients. The study population consisted of 150 subjects, age and sex-matched and divided into three groups [control subjects (n=50), HIV infected (n=50) and AIDS patients (n=50)]. Serum levels of total cholesterol, high-density lipoprotein cholesterol (HDL-C) and low-density lipoprotein cholesterol (LDL-C) were found to be decreased significantly in HIV/AIDS patients when compared with normal counterparts. On the other hand, the levels of triglyceride (TG) and very low-density lipoprotein cholesterol (VLDL-C) were markedly elevated in HIV/AIDS patients compared to normal subjects. The activities of serum aspartate aminotransferase (AST), alanine aminotransferase (ALT) and alkaline phosphatase (ALP) observed in HIV/AIDS patients were significantly higher than in the control group. Further, the above mentioned biochemical variables were found to be affected more significantly in AIDS patients when compared with HIV infected subjects. Hence, it may be concluded that lipid profile and liver enzymes can be a good index of disease progression in HIV infection and AIDS patients.

Index Terms- HIV-AIDS-Lipids-Liver Enzyme

I. INTRODUCTION

The acquired immunodeficiency syndrome (AIDS), is a fatal illness caused by a retrovirus known as the human immunodeficiency virus that breaks down the body's immune system, progressively leads to AIDS (Rasool et al. 2008). There are 2.47 million persons in India living with HIV; equivalent to approximately 0.36% of the adult population. The revised national estimate reflects the availability of improved data rather than a Substantial decrease in actual HIV prevalence in India. The transmission route is still predominantly sexual (87.4%); other routes of transmission by order of proportion include prenatal (4.7%), unsafe blood and blood products (1.7%), infected needles and syringes (1.8%) and unspecified routes of transmission (4.1%) (UNAIDS 2006).

Men with HIV infection were reported to have hypocholesterolaemia with and without hypertriglyceridaemia (Grunfeld et al. 1991, National AIDS Control Organization - NACO 2003, Anastos et al. 2007). An association between pla s m a t r i g l y c e ride and circulating interferon-levels has been observed in persons with AIDS. However, the mechanism for hypocholesterolaemia in HIV and other infections is not known. A pattern of hyperlipidaemia (i.e. elevated levels of total cholesterol, low-density lipoprotein cholesterol, and triglycerides, and a reduced level of high-density lipoprotein cholesterol) has been observed in patients treated with protease inhibitors (Crook and Mir 1999, Ducobu and Payen 2000, Khiangte et al. 2007). Infection can increase plasma triglyceride levels by decreasing the clearance of circulating lipoproteins, a process considered to be the result of reduced lipoprotein lipase (LPL) or by stimulating hepatic lipid synthesis through increases in either hepatic fatty acid synthesis or re-esterification of fatty acid derived from lipolysis (Grunfeld et al. 1992). Hypertriglyceridaemia was the first dyslipidaemia to be reported in HIV infected patients, but other lipid abnormalities such as hypocholesterolaemia or hypo HDL cholesterolaemia have also been reported. Although immunological dysfunction is common to all AIDS patients, the clinical spectrum of HIV infection is diverse and multiple organ involvement is frequently evident (Dalgleish et al. 1984). Liver disease has been linked to HIV infection and may manifest as fever of unknown origin, hepatomegaly or sub-clinical abnormalities in liver function tests (Tietz et al. 1983, Montagnier et al. 1984).

Studies also suggested that the major cause of hepatitis in HIV patients is infection by a secondary virus called the cytomegalo virus. It is also of interest that HIV has been detected in the liver cells of AIDS patients. It may be that those cells targeted for apoptosis are the same cells infected with HIV (Cooper et al. 1984).

In various forms of liver disease, serum levels of numerous cytosolic, mitochondria and membrane-associated enzymes are increased. The degree of elevation varies with the type of disease. Alanine and aspartate aminotransferases and alkaline phosphatase are the enzymes that are most often measured for evaluation of liver disease or diseases affecting the liver or in diseases where the liver is implicated (Tietz et al. 1983). The knowledge of the intracellular location of enzymes can therefore assist in determination of the nature and severity of a pathological process if suitable enzymes are assayed in the blood. The present study was undertaken to find out the relationship between changes in lipid profile and liver marker enzymes in HIV infection and AIDS patients.

II. MATERIALS AND METHODS

Study population

The population was selected consisting of 150 subjects divided into three groups: HIV infected patients 50 cases (n=50), AIDS patients 50 cases (n=50) and an equal number of age - and sex- matched control subjects (n=50). The study was carried out at the Shri Vasantrao Naik Govrment Medical College, Yavatmal, Maharashtra, India from January 2012 to January

2014. For diagnosis and confirmation of HIV infection, we followed the National AIDS Control Organization (NACO) recommendations for HIV testing (NACO 2003). All the patients were subjected to detailed history taking and clinical examination. The informed consent of the patients was obtained before testing.

Biochemical investigation

Fasting blood glucose, serum total cholesterol, triglyceride, HDL, LDL and serum enzymes (AST, ALT and ALP) were estimated by a fully automated clinical chemistry analyzer (240 Nano Lab Trivitron). VLDL cholesterol was calculated by the Friedewald equation.

Statistical analysis

All data were expressed as mean ± SD. The statistical significance was evaluated by student 't' test (two-tailed). A p value of <0.05 was considered statistically significant. Statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS Cary, NC, USA) version 10.0.

III. RESULTS

Information about the investigated characteristics is shown in Table 1. The mean age limit was 36 ± 9 in AIDS patients, 32 ± 5 in HIV infected patients and 30 ± 6 in control subjects. The decreased body mass index in AIDS patients (25 ± 5.3 kg/m^2) compared with HIV infected patients (29 ± 6.2 kg/m^2) and control subjects (34 ± 6.2 kg/m^2) were statistically significant. There was an increased number of hypertension sufferers and smokers observed in AIDS patients compared with HIV infection and control subjects. Diabetic participants were defined as those with a fasting blood glucose concentration >120 mg/dl.

The plasma concentrations of lipids (total cholesterol, triglyceride, HDL, LDL and VLDL) and serum enzymes (AST, ALT and ALP) in control and HIV infected and AIDS patients are depicted in Table 2. The levels of total cholesterol, HDL and LDL were significantly decreased, while the level of triglyceride and VLDL were significantly increased in AIDS patients when compared to HIV infected patients and normal subjects, but the levels of VLDL in the HIV infected patients and control subjects did not differ significantly. The activities of serum liver marker enzymes observed in AIDS patients significantly increased in the HIV infection patients and control subjects, The above biochemical variables were found to be altered more significantly in AIDS patients when compare with HIV infected subjects.

IV. DISCUSSION

The present study showed that the lipid profile was altered in HIV infected and AIDS patients. Alteration in the lipid profile occurred even during the early stages of HIV infection and more so as the disease progressed. Of the total 50 cases, 46 (92%) were classified as having AIDS according to Clinical Case Definition of AIDS. This high number of AIDS cases and the fact that there were no patients in the clinical stage in our study could be due to the fact that patients with HIV infection seek hospital admission only in the late clinical stages when they have opportunistic infections (NACO 2003).

Previous studies have demonstrated that patients with AIDS exhibit highly abnormal total lipid concentrations in plasma (Mullamitha and Pazare 1999). A few authors have determined the levels of plasma triglycerides, total cholesterol and HDL cholesterol in HIV infected individuals by the level of immunological deficiency according to they also came to the same conclusion: with an increase of immunological deficiency and clinical development of HIV infection, lipid profile disorders – indicated by an increase in triglyceride level and decreased concentrations of HDL cholesterol – also intensified (Rogowska-Szadkowska and Borzuchowska 1999, Ducobu and Payen 2000). Consistent with earlier reports, our study also showed similar findings in which the decrease due to disease progression was accompanied by a decrease in total cholesterol, HDL and LDL, and an increase in triglyceride and VLDL levels.

Our findings are also consistent with reports from Ducobu and Payen (2000), who stated that HIV infection induced an early decrease of cholesterol and a late increase of triglyceride with a reduction of HDL. Reported that patients with AIDS had increased levels of LDL cholesterol, which contradicted our findings. Shor Posner et al. (1995)

Reported similar findings in which they showed significantly low levels of total cholesterol, HDL and LDL in HIV infected patients, and about 40% of the HIV-infected subjects were demonstrated hypocholesterolaemic when compared to seronegative controls.

Table 1. Demographic characteristics of control, HIV infection and AIDS patiens

Characteristic	Control subjects	HIV infection	AIDS patients
Age (years)	30 ± 6	32 ± 5	36 ± 9* ^{x}
Sex (Male)	50	50	50
Body mass index (kg/ m^2)	34 ± 6.5	29 ± 6.2^{xx}	25 ± 7.1*^{x}
Number of subjects with			
Smoking	10 (20%)	27 (54%)	29 (58%)

Hypertension	4	(8%)	25 (56%)	43 (86%)
diabetes mellitus		-	8 (16%)	12 (24%)

Values are given as mean ± S.D. from 50 patients

*AIDS patients statistically significant as compared with control subjects ^{xx} HIV infection statistically significant as compared with control subjects ^{x} AIDS patients statistically significant as compared with HIV infection

Table 2. Changes in the level of total cholesterol, triglyceride, HDL, LDL, VLDL and serum enzymes in control, HIV infection and AIDS patiens

Characteristic	Control subjects	HIV infection	AIDS patients
Total cholesterol (mg/dl)	148 ± 23.4	136 ± 25.0^{xx}	120 ± 27.6*^{x}
Triglyceride (mg/dl)	115 ± 24.6	201 ± 20.0^{xx}	392 ± 35.6*^{x}
HDL (mg/dl)	56 ± 7.2	43 ± 5.8^{xx}	20 ± 9.6*^{x}
LDL (mg/dl)	62 ± 17.2	53 ± 15.3^{xx}	45 ± 21.6*^{x}
VLDL (mg/dl)	23 ± 17	20 ± 13.0^{NS}	78 ± 15*^{x}
AST (IU/l)	20 ± 9.3	39 ± 10.0^{xx}	80 ± 28.6*^{x}
ALT (IU/l)	17 ± 9.6	73 ± 13.2^{xx}	175 ± 22.6*^{x}
ALP (IU/l)	75 ± 22.8	180 ± 20.4^{xx}	216 ± 28.6*^{x}

Symbols as in Table 1

This low level of total cholesterol, HDL and LDL was reported to be associated with elevated levels of β-2 microglobulin. Low cholesterol levels are prevalent even during the early stages of HIV and associated with a specific alteration in immune function. Kereveur et al . (1996) stated that hypocholesterolaemia observed in the early and hypertriglyceridaemia in the later stage of the infection are due to cytokine effects on different enzymes of lipid metabolism.

Grunfeld etal. (1991) has reported that HIV/AIDS is characterized by a high prevalence of hypertriglyceridaemia and hypocholesterolaemia, and also an elevated level of cytokines. They observed that decreased cholesterol and cholesterol containing lipoproteins in both AIDS and HIV infection precede the appearance of hypertriglyceridaemia. Increased TG levels in AIDS were primarily due to an increase in VLDLThey also raised the possibility that with the development of AIDS, subsequent increase in IFN may have contributed to an increase in plasma triglyceride levels by decreasing the clearance of TG. The increase of triglyceride catabolism in relation to a reduction of lipoprotein lipase activity was responsible for these lipid changes. Many cytokines such as IFN, IL and TNF probably play a pathogenic role in the dyslipedaemia of HIV (Rogowska-Szadkowska and Borzuchowska 1999). Hence, it may be suggested that the lipid profile can be a good index of disease progression in HIV infection and AIDS patients.

In this study, we noticed a significant increase in serum liver marker enzymes (ALT, AST and ALP) in HIV/AIDS patients compared with the control group. Our results are also consistent with the earlier findings of Wildup etal. (1993) who recorded a significant increase in the activities of the three afore-mentioned enzymes investigated. It is of interest to note that HIV has been detected in the liver cells with noticeable pathogenesis of the affected cells in infected individuals and since HIV infection and AIDS patients tend to suffer more chronic, unrelenting forms of many secondary diseases, it is therefore likely that the liver too will be affected and that subsequently changes will occur in the activities of the liver enzymes in HIV infection and AIDS patients. HIV attack host cells and take over the control of the infected cells leading to eventual death of the cells and subsequently the release of cellular contents into the surrounding medium of which enzymes constitute 20%. This may be responsible for the increase in the level of liver enzymes in infected liver cells. Changes in the three mentioned liver enzymes should not be surprising since it is likely that an intact immune response to viral replications is necessary to produce the hepatocellular necrosis and inflammation seen in active hepatitis due to HIV infection and AIDS.

Other causes of increased serum enzymes include: hepatitis due to hepatitis B virus, HCV, drug toxicity, extra-hepatic cholestasis, cirrhosis, hepatobiliary disease, genetic abnormalities with increased production of enzymes, enzyme induction and proliferation of enzyme producing cells, for example, in cancer patients, but these conditions were not exhibited in the patients examined. It is possible nonetheless, that these other conditions could be secondary to HIV infection and thus contribute to an increase in the activities of the liver enzymes examined perhaps to different degrees (Oguntibeju and Banjoko 2003). A detailed analysis, which could include differential enzyme studies, could clarify other sources of ALT, AST and ALP increase in serum. From these findings it therefore becomes necessary to estimate serum levels of ALT, AST and ALP, other liver enzymes and isoenzymes in HIV and AIDS patients to be able to at least monitor prognosis and progressive involvement of the liver cells. This would require continuous monitoring of the patient. In such a case, a sharp increase from the steady state concentrations in a particular patient may be an indication of early or late involvement of the liver cells either mildly or severely in the absence of other known causes. It is likely that the changes in biochemical parameters induced by HIV infection will have biological and possibly pathological importance in the development of AIDS and related complications. It is also recommended that the results obtained in this study be used as baseline in the pre-intervention and subsequent management of HIV infection and AIDS patients.

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AUTHORS

First Author –Mahendra R. Pakhale, M.Sc.Medical Biochemistry, Assit. Professor & Lab Incharge , Dept. Of Biochemistry, S.V.N.Govt. Medical College,Yavatmal (MS), Mobile No-8983813183, E-mail-mahe1426@yahoo.co.in
Second Author – Dr. Trupti Ramteke, MD-Biochemistry

Assit. Professor, Dept.of Biochemistry, S.V.N.Govt. Medical College,Yavatmal (MS)

Third Author – Dr.Arun Tadas, MD-Biochemistry, Professor & HOD Dept, of Biochemistry, S.V.N.Govt.Medical College Yavatmal (MS)