Abnormalities of liver enzymes in HIV positive patients on antiretroviral therapy

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Abstract

Introduction: Liver disease is considered as one of the main health concern in Human Immunodeficiency Virus (HIV) patients. Diseases of the liver in HIV patients encompass spectrum of liver abnormalities. Elevated levels of liver enzymes like aspartate transaminase (AST), alanine transaminase (ALT) and alkaline Phosphatase (ALP) are markers of hepatocyte injury. The aim of the present study was to evaluate the clinical significance of liver enzymes such as AST, ALT and ALP in HIV patients on antiretroviral therapy.

Materials and Methods: In this cross sectional case-control study, a total of 180 subjects were included in this study. Among them 90 HIV positive patients were included as cases and 90 normal subjects were included as controls. Seropositivity of all 90 HIV patients was confirmed by HIV TRI-DOT test. Estimation of serum AST, ALT and ALP was done by using automated chemistry analyzer. P value <0.001 is considered as significant.

Results: In this study, there is a significant elevation in liver enzymes such as AST, ALT and ALP ($p<0.001$) in HIV positive cases when compared to healthy controls.

Conclusion: In this study, we conclude that, significantly elevated levels of liver enzymes is observed in HIV positive patients under the treatment. Therefore, the elevated levels of liver enzymes should be analyzed and monitored in HIV patients to prevent further progression of disease.

Keywords: CD4+ cells, Liver disease, HIV, Hepatotoxicity, Anti-retroviral therapy.

Introduction

Liver is a major part of the reticulo-endothelial system. It is a site of HIV replication and organ for many opportunistic infections.[1] Globally, 40 million people are infected with HIV and the disease burden in more in low and middle income countries.[2,3] HIV is now epidemic in India and it was first recognized in 1986. In India, 5.2 million of people are affected by HIV infection and has the second highest number of these patients in the world.[3]

Hepatobiliary system diseases are the main health issues in HIV infected patients globally. HIV is a retrovirus, but differs from other retroviruses such as human T lymphotrophic viruses (HTLV) 1 and 2. HIV is generally present as a virion (either cell-associated or cell-free) and it is detected clearly in a majority of cells, whereas HTLVs detected in their target cells. The main reasons for the transmission of HIV infection is direct exposure to blood and blood products, male and female genital secretions, or breast milk. Pregnant women can pass the HIV to the fetus through the placenta. Three main body systems usually affected by AIDS are the respiratory system, gastrointestinal tract and central nervous system. Most of these conditions are due to reactivation of latent organisms in the patient or exposure to numerous microbial flora in the environment.[4]

The liver disease in HIV infection involves spectrum of liver abnormalities, including abnormal liver function tests, decompensation of liver cells, liver cirrhosis with and without evidence of on biopsy, to NAFLD and more severe forms of NASH and hepatocellular carcinoma. Hepatitis B virus (HBV) and hepatitis C (HCV) infections, chronic alcoholism and TB can also cause liver disease in HIV patients.[3]

Liver function in HIV infected patients may be altered either direct or indirect mechanisms. CD4+ cells, monocyte/macrophages and dendritic cells are mainly affected by HIV. HIV directly damages liver cells leading to apoptosis and mitochondrial dysfunction. The inflammatory mechanism is exaggerated by HIV infection due to permeability alteration in mitochondrial membrane.[5,6] Liver enzymes could be used as markers for hepatic injury.[6] The aim of the present study was to evaluate the clinical significance of liver enzymes such as AST/SGOT, ALT/SGPT and ALP in HIV patients on antiretroviral therapy.

Materials and Methods

Study design is cross sectional case-control study, conducted at Department of Biochemistry, NRI Medical College & General Hospital, Chinnakakani, Guntur, Andhra Pradesh. A total of 180 subjects were included in this study. Among them 90 HIV positive patients were included as cases and 90 healthy subjects were served as controls. Age of the subjects was between 20 to 60 years. After explaining the study procedure and fulfilling the inclusion and exclusion criteria the subjects were recruited into the study. Patients with congestive heart failure, liver diseases, diabetes and HTN were excluded from the study. The physical and clinical examination was done for all the study subjects. In a plain vacuum tube 5 ml of venous blood sample was collected, incubated for 20 minutes and centrifuged at 3000 rpm for 5 minutes to obtain clear serum.

Estimation of serum AST, ALT, ALP done by using automated chemistry analyzer Dade Behring Dimension RXL Chemistry Analyzer. The study was approved by institutional ethical committee and informed consent was obtained from the study subjects.

Statistical Analysis

Data were expressed as mean ±SD. P value <0.001 is considered as significant. Data analysis was done by using SPSS, version 20.0, Graph pad calculator software.

Results and Discussions

In this study, total number of subjects was 180. Total of 90 HIV positive patients were selected as cases and 90 healthy subjects were controls. Mean age and sex distribution of the study subjects was shown in Table 1. In this study, there is a significantly elevated level of liver enzymes such as AST, ALT and ALP (p<0.001) observed in HIV patients when compared to controls, as illustrated in Table 2.

Table 1: Age and sex distribution in control and cases

	No. of Males	No. of Females
Control (90)	40 (44.4%)	50 (55.5%)
HIV positive patients (90)	37 (41.1%)	53 (58.8%)

Table 2: Comparison of liver enzymes between healthy controls and HIV patients

Parameters	Controls (n=90) Mean ± SD	Cases(n= 90) Mean ± SD	P-value
AST (IU/L)	28.3±7.68	46.9±6.68	<0.0001*
ALT(IU/L)	35.07±6.75	60.06±10.72	<0.0001*
ALP(IU/L)	182.67±53.89	257.56±67.15	<0.001*

***** Statistically significant

Discussion

In the present study, significantly elevated levels of liver enzymes such as aspartate transaminase (46.9±6.68), alanine transaminase (60.06±10.72) and alkaline phosphatase (257.56±67.15) were observed. HIV directly damages the liver cells leading to apoptosis and mitochondrial dysfunction. The exact mechanism for the hepatic disease in HIV infected patients is unknown and it has to be explored.[5,7] Liver diseases, especially hepatic carcinoma, is a major health issue in HIV infected individuals. HIV infection has been shown to alter the normal functioning of the liver cells. Studies have shown that, the HIV predominantly infects CD4+ T-cells, monocyte/macrophages and dendritic cells.[8,9] In vivo, studies have reported that, in the sinusoidal cells and hepatocytes HIV RNA has been detected.[10,11] Primary human sinusoidal cells have also been shown to be permissive to HIV infection. Hepatic infection is thought to be CD4 dependent as most hepatocyte cell lines, and primary hepatocytes, do not express CD4. Hence, the receptor – mediated endocytosis or alternative co-receptors are involved in the hepatic infection by HIV.[12] Liver cells may also act as a transient HIV reservoir and promote CD4+ T cell infection by cell-cell contact.[13] Liver cell apoptosis can also be induced by HIV, in the absence of hepatic infection. Apoptosis of liver cells can enhance the hepatic stellate cells (HSC) pro-fibrotic activity. Studies have demonstrated this in both HIV co-infection with HBV and HCV.[14,15]

HIV infection or the presence of opportunistic infections is known to stimulate an immunological response by hepatic phagocytes against the infection. Some liver diseases are often linked with HIV infection leading to increased transaminases. Increased levels of liver enzyme due to other causes such as acute viral hepatitis, reconstitution of chronic hepatitis B or C, alcohol ingestion as well as complementary drugs or medicines associated with ART have been reported. Patients included in this study did not have hepatitis B and C infection. This study results are supported by Ogunro PS et al and Schniedermann D et al.[16,17]

Conclusion

In the present study, significantly elevated levels of liver enzymes such as AST, ALT and ALP were observed in HIV positive patients under treatment. The high levels of hepatic enzymes in HIV positive patients may be considered as a prognostic markers and high levels of this hepatic enzymes had poor prognosis in HIV patients. Hence, hepatic enzyme estimation may be beneficial in HIV positive patients and these enzymes should be monitorized to prevent further hepatic damage. Limitations of the study include small sample size. Future large prospective studies are recommended to improve recognition, diagnosis and effective management of hepatic damage in HIV patients and to assess antiretroviral therapy effects on liver. Antiretroviral drugs which are not hepatotoxic should be developed.

Conflict of Interest: Nil

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