

## LIVER FUNCTION ABNORMALITIES IN HIV POSITIVE INDIVIDUALS WITH VIRAL HEPATITIS CO-INFECTION

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**ABSTRACT: BACKGROUND:** Liver enzyme elevations are common in human immunodeficiency virus (HIV)-infected patients, and their diagnosis and management becomes a challenge because of complex pathogenic mechanisms. Liver enzyme abnormalities may be worsened by hepatitis B (HBV) or hepatitis C (HCV) infection, which each have their own risks for chronic immune-mediated liver disease along with direct cytotoxicity.

**OBJECTIVES:** The present study was done to identify various liver function abnormalities in HIV and viral hepatitis co-infection

**METHODS:** The study included 22 HIV seropositive patients along with serology positive for hepatitis (19 patients were HBsAg positive and 3 patients were HCV positive) who presented to Sri Ramachandra Medical College and Hospital from the year 2012 to 2014. Complete haemogram, blood urea, serum creatinine, liver function tests, CD4 count, and ultrasound abdomen was done for all the patients. LFT abnormalities were compared with HIV positive patients without hepatitis (78 patients).

**RESULTS:** LFT abnormalities were significant in comparison to patients with negative hepatitis serology. Only a modest elevation of liver enzymes was seen in hepatitis. Co-infection. Majority of the patients had elevation of transaminases and INR was normal in all HCV positive patients.

**CONCLUSION:** HBV and HCV coinfection increases the incidence of LFT abnormality. Only a modest elevation of liver enzymes was seen in hepatitis co-infection.

**KEYWORDS:** HIV Infection, Viral Hepatitis, Liver Function.

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**INTRODUCTION:** Liver enzyme elevations are common in human immunodeficiency virus (HIV)-infected patients, and their diagnosis and management becomes a challenge because of complex pathogenic mechanisms. Hepatotoxicity related to the highly active antiretroviral therapy (HAART) regimen, idiosyncratic or immunoallergic mechanisms, and direct cytotoxicity enhanced by an underlying liver disease all contribute to liver injury. Liver enzyme abnormalities may be worsened by hepatitis B (HBV) or hepatitis C (HCV) infection, which each have their own risks for chronic immune-mediated liver disease along with direct cytotoxicity.<sup>[1]</sup> At the beginning of the AIDS era, liver dysfunction in HIV -infected patients mainly corresponded with opportunistic infections (e.g., with cytomegalovirus [CMV], mycobacteria, leishmaniasis, cryptosporidiosis and microsporidiosis), tumors (Lymphoma and Kaposi sarcoma); and drug-related hepatitis (Caused by trimetoprim-sulfamethoxazole and other antibiotics).

HAART has changed the pattern of hepatic events in HIV infection, and the liver is an important organ to consider when treating HIV-infected patients. Human immunodeficiency virus (HIV) infection of liver cells can contribute to liver disease progression by either direct or indirect mechanisms. HIV can directly infect hepatocytes, hepatic stellate cells (HSCs) and Kupffer cells (KCs). Glycoprotein120 binding to CXCR4 can induce hepatocyte apoptosis and activation of HSCs which in turn induce fibrosis. Nucleoside reverse transcriptase inhibitors (NRTIs) and HIV itself [Via peroxisome proliferator-activated receptor (PPAR) effects] may also contribute to liver disease by inducing the metabolic syndrome.

HIV infection of the gastrointestinal tract leads to an increase in lipopolysaccharide (LPS) which can stimulate hepatocytes, KCs and HSCs to produce pro-inflammatory cytokines and chemokines which attract activated lymphocytes and monocytes to the liver which may further drive fibrosis. HIV infection of the gastrointestinal tract leads to an increase in lipopolysaccharide (LPS) which can stimulate hepatocytes, KCs and HSCs to produce pro-inflammatory cytokines and chemokines which attract activated lymphocytes and monocytes to the liver which may further drive fibrosis.<sup>[2,3,4,5,6]</sup> Hepatocyte apoptosis can trigger pro-fibrotic activity of HSC, as has been demonstrated in both HIV-HBV co-infection and HIV-HCV co-infection.<sup>[7]</sup>

The exact role of HIV-induced hepatic cell apoptosis and liver disease needs to be determined by further studies. The present study was done to identify various liver function abnormalities in HIV and viral hepatitis co infection.

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**MATERIAL AND METHODS:** The study included 22 HIV positive patients along with serology positive for hepatitis (19 patients were HBsAg positive and 3 patients were HCV positive) presented to Sri Ramachandra Medical College and Hospital from the year 2012 to 2014, after approval of Hospital ethics committee. All patients fulfilling inclusion criteria (All HIV seropositive patients with serology positive for hepatitis B or C confirmed by ELISA) were screened and investigations done. Patients with age less than 18 years and pregnant patients were excluded from the study.

A questionnaire for detailed history was taken from all patients and physical examination was done. A thorough abdomen examination to demonstrate hepatomegaly, splenomegaly, free fluid, cirrhosis of liver was carried out. Complete blood count, blood urea, sugar, serum creatinine, liver function tests including coagulation profile and urine analysis were done for all patients. The CD4 lymphocyte count was done by flow cytometry method. Abnormal liver function tests were defined as >1.25 ULN in HIV positive patients. The data were compared with HIV positive patients without hepatitis (78 patients).

The collected data was analyzed using Statistical Package of Social Sciences (SPSS) 17.0 for windows. Data were expressed as the mean + standard deviation. A p value of less than 0.05 was considered statistically significant.

**RESULTS:** The study included 19 patients with HBsAg positive and 3 patients with HCV positive. 78 patients had serology negative for hepatitis B or C. Various liver parameters were analysed in patients with hepatitis co-infection and data compared with patients having no hepatitis. The results are summarised in tables 1 and 2. Only SGOT elevation in hepatitis B co-infection had statistical significance.

**DISCUSSION:** The study was done to ascertain whether LFT abnormalities would be significantly affected with hepatitis co-infection. Direct injury by HIV can cause abnormal liver function. Co-infection with viral hepatitis could further worsen the liver function. In the present study 19 patients (19%) were positive for HBV surface antigen and 3 patients (3%) had antibodies to HCV.

In the study by Richard K. Sterling et al.<sup>[8]</sup> 7.1% patients were positive for HBV surface antigen and 24% patients had antibodies to HCV. In the study by Ejilemele AA et al.<sup>[9]</sup> 2.3% were HBsAg positive and 0.8% patients had antibodies to HCV. In the study done by Ponsiano Ocama et al.<sup>[10]</sup> 15% patients were HBsAg positive and 3% patients had antibodies to HCV. In our study the prevalence of those with HBV and HCV was SGOT-89.5%, SGPT-73.7%, ALP-52.6% compared to SGOT-61.7%, SGPT-56.8%, ALP-32.1% in those without HBV and HCV co-infection.

In the study done by Richard K. Sterling et al. the prevalence of those with HBV and HCV was SGOT - 64%, SGPT-46%, ALP-63% compared to SGOT-20%, SGPT-15%, ALP- 43% in those without HBV and HCV co-infection.

In our study there was a statistically significant relationship between Hepatitis B positive status and SGOT elevation (p-value- 0.021).

**CONCLUSION:** LFT abnormalities were significant in comparison to patients with negative hepatitis serology. Only a modest elevation of liver enzymes was seen in hepatitis co-infection. HBV and HCV co-infection increases the incidence of LFT abnormality.

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Parameter	Hepatitis B Negative	Hepatitis B Positive	P value
Bilirubin < 1.5	72	16	0.572
Bilirubin > 1.5	9	3	0.572
SGOT < 44	31	2	0.021
SGOT > 44	50	17	0.021
SGPT < 51	35	5	0.176
SGPT > 51	46	14	0.176
Alkaline phosphatase < 161	55	9	0.803
Alkaline phosphatase > 161	26	10	0.803
INR < 1.1	53	12	0.952
INR > 1.1	28	7	0.952
Albumin > 3.2	51	10	0.406
Albumin < 3.2	30	9	0.406

**Table 1: HIV and Hepatitis B co-infection**

LFT elevations were significant in patients with hepatitis B co-infection. Statistical significance was seen only for SGOT.

Parameter	Hepatitis C Negative	Hepatitis C Positive	P value
Bilirubin < 1.5	85	3	0.566
Bilirubin > 1.5	12	0	0.566
SGOT < 44	32	1	0.990
SGOT > 44	65	2	0.990
SGPT < 51	38	2	0.338
SGPT > 51	59	1	0.338
Alkaline phosphatase < 161	62	2	0.992
Alkaline phosphatase > 161	35	1	0.992
INR < 1.1	62	3	0.197
INR > 1.1	35	0	0.197
Albumin > 3.2	60	1	0.318
Albumin < 3.2	37	2	0.318

**Table 2: HIV and Hepatitis C co-infection**

The analysed data showed that LFT abnormalities were not statistically significant in HCV co-infection.