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Original Article

A cross-sectional study of liver function tests in HIV-infected persons in Western India

Maj Sunny Pathania [a], *Sqn Ldr Navjyot Kaur* [b], *Maj Sandeep Kumar* [c], *Air Cmde V.K. Sashindran* [d,*], *Brig Pankaj Puri* [e]

[a] *Resident, Department of Medicine, Armed Forces Medical College, Pune 411040, India*
[b] *Assistant Professor (Medicine), Command Hospital (Southern Command), Pune 411040, India*
[c] *Assistant Professor, Department of Medicine, Armed Forces Medical College, Pune 411040, India*
[d] *Professor & Head, Department of Geriatric Medicine, Armed Forces Medical College, Pune 411040, India*
[e] *Professor & Head, Department of Internal Medicine, Armed Forces Medical College, Pune 411040, India*

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ABSTRACT

Background: Derangement of liver function tests (LFTs) is common in people living with human immunodeficiency virus/acquired immune deficiency syndrome (PLHA). The cause is multifactorial. Drug-induced liver injury (DILI) is the commonest cause and others being alcohol abuse and concomitant viral hepatitis. The aim of the research was to study the prevalence of LFT abnormalities in PLHA.

Methods: The study was carried out in a tertiary care hospital. Evaluation included a detailed history, thorough clinical examination and investigations including a haemogram, serum biochemistry, serology for hepatitis, and CD4 cell count.

Results: A total of 247 patients were evaluated. Of these, 212 (85.82%) were on antiretroviral therapy (ART), 111 (44.93%) were on anti-tubercular therapy (ATT), and 94 (38.05%) were on concurrent ATT–ART.

Abnormal LFTs were seen in 128/247 (51.82%) PLHA. In the majority (88.28%), the LFT abnormalities were mild. LFT abnormalities were seen in 109/212 (51.4%) patients on ART, in 56/111 (50.5%) patients on ATT, 46/94 (48.93%) patients on concurrent ART–ATT. There was no difference in LFT abnormalities among the three groups nor was there any significant association with alcohol consumption. There was a statistically significant co-relation between albumin/globulin ratio and CD4 count ($p = 0.0002$). Counter-intuitively, LFT abnormalities were commoner in patients not receiving nevirapine ($p = 0.043$), but severe abnormalities (grade III/grade IV) were commoner in those receiving nevirapine ($p = 0.005$) and in those on concurrent ART–ATT ($p = 0.008$).

Conclusion: LFT abnormalities in PLHA are common; but usually mild. There is a strong association between severe abnormalities and nevirapine-based therapy ($p = 0.02$) and concurrent ATT–ART ($p = 0.008$).

* *Corresponding author*. Tel.: +91 9673113005.
E-mail address: vksashindran@gmail.com (V.K. Sashindran).

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Introduction

Liver function test (LFT) abnormalities are widely prevalent in people living with human immunodeficiency virus/acquired immune deficiency syndrome (PLHA) and have been reported anywhere between 20 and 93%.[1,2] In fact liver diseases account for almost 14–18% of all deaths in PLHA.[3] In some series, nearly half of the deaths among hospitalized human immunodeficiency virus (HIV)-infected patients have been attributed to liver disease.[4–6] The important causes of liver dysfunction among HIV-infected individuals are concomitant infection with hepatitis C virus (HCV), hepatitis B virus (HBV), medication-related hepatotoxicity, alcohol abuse, and non-alcoholic fatty liver disease (NAFLD).[7–10]

PLHA are usually on multiple drugs like antiretroviral therapy (ART), anti-tubercular therapy (ATT) and cotrimoxazole which are all potentially hepatotoxic. Due to their poor immune status, they are prone to various bacterial, viral and fungal infections and are also prescribed many other antibiotics, antifungals and antivirals as the clinical condition warrants. This poly-therapy in PLHA makes them very prone to drug-induced liver injury (DILI). HBV and HCV have the same mode of transmission as HIV; and therefore the prevalence of infection by these hepatotropic viruses in PLHA is more than in general population. In studies from the West, past HBV infection (IgG anti-HBc positive) has been documented in 80–90% of patients infected with HIV[11–13] and the overall prevalence of HCV infection in HIV is estimated to be around 30%.[14–16] Indian studies have documented the prevalence of HCV in PLHA between 1.3% and 8.3%.[17–19]

Many PLHA consume significant amounts of alcohol which can have more than additive effect in causing liver dysfunction along with ART and ATT. To add on, certain conditions specific to HIV like opportunistic infections with cytomegalovirus, cryptosporiodosis, disseminated fungal and mycobacterial infection, HIV cholangiopathy, and lymphomas; all can cause LFT abnormalities.[3,20,21] Nowadays with better care and effective ART, PLHA live longer and hence also develop diseases of old age like metabolic syndrome which is further aggravated by some ART drugs especially protease inhibitors. Hence, NAFLD is also increasingly being encountered in these patients.

This study was carried out with an aim to study the prevalence of LFT abnormalities in PLHA at an ART centre of Pune, Maharashtra.

Material and methods

This cross-sectional observational study was carried out among HIV-infected persons at an ART centre in Pune, Maharashtra. HIV positive cases diagnosed as per National AIDS Control Organization (NACO) guidelines were included. Pregnant and lactating females and children less than 12 years were excluded. Informed consent was obtained from each individual. The sample size required for estimating the prevalence of LFT abnormalities in HIV patients with 95% confidence interval and precision of 5% around true prevalence ranging from 20% to 93%[1,2] was 246 patients.

Detailed history was taken from all patients with special reference to duration of HIV infection, alcohol consumption and medication including ART, ATT, cotrimoxazole and other potentially hepatotoxic drugs. Excessive alcohol use was defined as more than 20 g of ethanol per day for men and more than 10 g of ethanol per day for women. A thorough clinical examination was carried out on all patients.

Investigations done in all patients included complete blood count, CD4 count, hepatitis B surface antigen (HBsAg), antibodies against hepatitis C virus (anti-HCV antibodies), lipid profile, blood sugar levels and LFTs. The LFTs included serum bilirubin, aspartate aminotransferase (AST), alanine aminotransferase (ALT), serum alkaline phosphatase (SAP), serum albumin and globulin. Grading of LFT abnormalities was done as per AIDS Clinical Trial Group[22] as per Table 1. Grade 3 and 4 abnormalities were considered as 'severe' LFT abnormalities. A patient was diagnosed to have metabolic syndrome if he/she had any three of the following abnormalities: BMI > 25 kg/m^2, HDL < 40 mg/dL (in males) or <50 mg/dL (in females), triglycerides >150 mg/dL, hypertension, or fasting blood sugar >100 mg/dL.

Statistical analysis

Frequency tables and cross tabulation were used to evaluate the factors associated with liver enzymes abnormalities. Univariate models were used to examine each variable with the presence of any abnormal liver test. Cross tabulation was also used to compare those with and without liver function abnormalities, and to compare different variables. Tests for significant difference in means and proportions for various parameters were done. A p value of less than 0.05 was considered to be statistically significant.

Table 1 – Grades of liver dysfunction.

	Grade 1	Grade 2	Grade 3	Grade 4
ALT	1.25–2.5 ULN (50–100 IU/L)	2.6–5 ULN (101–200 IU/L)	5–10 ULN (201–400 IU/L)	>10 ULN (>400 IU/L)
AST	1.25–2.5 ULN (50–100 IU/L)	2.6–5 ULN (101–200 IU/L)	5–10 ULN (201–400 IU/L)	>10 ULN (>400 IU/L)
SAP	1.25–2.5 ULN	2.6–5 ULN	5–10 ULN	>10 ULN
Bilirubin (mg/dL)	1–1.5	1.6–2.5	2.6–5	>5

ALT, alanine aminotransferase; AST, aspartate aminotransferase; SAP, serum alkaline phosphatase; ULN, upper limit of normal; IU, international units.