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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 (grade III/grade IV) 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 ($p = 0.008$).

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* Corresponding author. Tel.: +91 9673113005.

E-mail address: vkashindran@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, cryptosporidiosis, 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 Group²² 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/m², 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.

Results

We evaluated 247 HIV positive patients (173 males, 74 females, mean age: 40.59 ± 11.20 years, average BMI: 20.02 ± 2.69 kg/m²). The mean CD4 count of our cohort was $353.55/\text{dL} \pm 315.92$ cells/ μL . A total of 212 (85.82%) patients were on ART, 111 (44.93%) patients were on ATT, 94 (38.05%) patients were on concurrent ATT-ART and 170 (68.82%) patients were receiving cotrimoxazole prophylaxis in addition to ART. Most patients on ART ($n = 200$) received a combination of two nucleoside/nucleotide reverse transcriptase inhibitors (NRTI) and one non-nucleoside reverse transcriptase inhibitor (NNRTI). The constant NRTI in all regimens was lamivudine. The other one varied and was either zidovudine (118)/tenofovir (88)/abacavir (5)/stavudine (1). The NNRTI in the ART regimen of these 200 patients was nevirapine ($n = 121$) or efavirenz ($n = 79$). Nine patients were on second-line ART and received ritonavir boosted lopinavir or atazanavir. In addition, three patients were on raltegravir therapy. These twelve patients were not on any NNRTIs.

Overall 128/247 patients (51.82%) had abnormal LFTs. Table 2 compares the characteristics of HIV-infected patients with or without abnormal LFT abnormalities.

Majority of the patients had mild abnormalities of transaminases (grade I in 92/128 [71.87%] patients, grade II in 29/128 [22.65%] patients) while significant rise was seen in only 7 patients (grade III in 6/128 [4.68%] patients, grade IV in only one patient). Hyperbilirubinemia was noticed in 27/247 (10.93%) patients. However, only 8 patients were icteric (grade III in 6 patients and grade IV in 2 patients). Only one patient had isolated rise in SAP (>3 times the upper limit of normal) which was due to granulomatous hepatitis.

LFT abnormalities were seen in 109/212 (51.4%) patients on ART (54/121 [44.6%] patients on nevirapine-based therapy and in 4/9 [44.4%] patients on protease inhibitors), 56/111 (50.5%) patients on ATT, 46/94 (48.93%) patients on ATT + ART and 85/170 (50%) patients on ART + cotrimoxazole. There was no difference in prevalence of LFT abnormalities among ART and non-ART groups ($p = 0.76$), ART and ATT-ART groups ($p = 0.52$), and ART and ART + cotrimoxazole groups ($p = 0.71$). While the LFT abnormalities were commoner in the group of patients who were not receiving nevirapine ($p = 0.043$), severe abnormalities (grade III/grade IV) were commoner in the group receiving nevirapine ($p = 0.02$). Severe LFT abnormalities were seen more frequently in patients on concurrent ATT-ART ($p = 0.008$). Table 3 demonstrates the LFT abnormalities in different subgroups.

Co-infection with hepatotropic viruses was noticed only in 3 patients (HBV-2, HCV-1). Significant alcohol intake was seen in 70 patients. There was no statistically significant association between HBV/HCV coinfection or alcohol use and higher prevalence of LFT abnormalities ($p > 0.05$). Using univariate analysis, it was seen that there was no co-relation of deranged LFT to CD4 values. The LFT abnormalities in CD4 count group >200 cells/ μL was 79/150 (52.7%) and in CD4 count <200 cells/ μL group was 49/97 (50.5%) and the difference was not significant (p value = 0.74). Metabolic syndrome was documented in 38 patients; and of these, 15 had abnormal LFTs (all grade I & II). A total of 21/38 patients had evidence of fatty liver on ultrasonography; out of these 6 were diagnosed to have NAFLD. The rest had history of significant alcohol consumption.

Overall severe LFT abnormalities were seen in 15 patients (12 males, 3 females, mean age: 40.6 ± 9.124 years, mean BMI: 20.28 ± 2.94 kg/m²). Mean CD4 count in this group was 225.33

Table 2 – Comparison of HIV-infected persons with or without abnormal LFT.

	LFT category		p value	Confidence interval
	Normal LFT ($n = 119$) Mean $\pm$ SD	Abnormal LFT ($n = 128$) Mean $\pm$ SD		
Age (years)	38.91 $\pm$ 11.41	42.156 $\pm$ 10.822	0.023	0.4596 to 6.0324
BMI (kg/m ²)	19.98 $\pm$ 2.65	20.0521 $\pm$ 2.637	0.851	–0.5909 to 0.7351
Duration of HIV (years)	6.61 $\pm$ 4.22	7.08 $\pm$ 4.246	0.381	–0.5919 to 1.5319
Duration of ART (years)	4.58 $\pm$ 3.59	4.109 $\pm$ 3.384	0.282	–1.3446 to 0.4026
Alcohol quantity (g/wk)	108.15 $\pm$ 104.68	113.460 $\pm$ 97.248	0.679	–19.9971 to 30.6171
Hb (g/dL)	10.91 $\pm$ 2.81	10.841 $\pm$ 2.698	0.830	–0.7594 to 0.6214
TLC (/dL)	5724.454 $\pm$ 1905.021	5874.453 $\pm$ 2268.759	0.576	–377.0911 to 677.0891
Platelet count (lakhs/ μL)	2.58 $\pm$ 1.28	1.588 $\pm$ 1.603	0.0001	–1.3573 to –0.6267
Bilirubin (mg/dL)	1.6287 $\pm$ 1.028	1.8252 $\pm$ 0.933	0.117	–0.0493 to 0.4423
AST (IU/L)	40.311 $\pm$ 34.294	48.711 $\pm$ 52.265	0.134	–2.7678 to 19.5678
ALT (IU/L)	36.454 $\pm$ 29.460	46.273 $\pm$ 44.203	0.040	0.3312 to 19.3068
ALP (IU/L)	106.552 $\pm$ 84.484	105.758 $\pm$ 59.878	0.932	–19.0477 to 17.4597
LDH (IU/L)	303.287 $\pm$ 172.385	316.523 $\pm$ 155.056	0.529	–27.8053 to 54.2773
Total proteins (g/dL)	6.661 $\pm$ 1.060	6.801 $\pm$ 0.928	0.272	–0.1093 to 0.3893
Albumin globulin ratio	1.2173 $\pm$ 0.385	1.1019 $\pm$ 0.469	0.037	–0.2234 to –0.0074
CD4 (cells/ μL)	348.6207 $\pm$ 326.488	351.5164 $\pm$ 330.462	0.951	–79.4948 to 85.2862
Blood sugar F (mg/dL)	93.1584 $\pm$ 13.081	99.6058 $\pm$ 32.420	0.044	0.1655 to 12.7293
Blood sugar PP (mg/dL)	122.8614 $\pm$ 17.632	130.9712 $\pm$ 42.588	0.055	–0.1694 to 16.3890

LFT, liver function tests; HIV, human immunodeficiency virus; ART, antiretroviral therapy; Hb, haemoglobin; TLC, total leucocyte count; ALT, alanine aminotransferase; AST, aspartate aminotransferase; SAP, serum alkaline phosphatase; LDH, lactate dehydrogenase; SD, standard deviation; IU, international units; F, Fasting; PP, post-prandial.

Table 3 – LFT abnormalities in various subgroups.

	LFT abnormalities	Proportion	
ART (212)	109	0.514	z score: -0.3149
No ART (35)	19	0.543	p value: 0.75656
Nevirapine based ART (121)	54	0.446	z score: -2.0197
Non-nevirapine based ART (94)	55	0.585	p value: 0.043
Only ART (118)	63	0.534	z score: 0.6446
Combined ART + ATT (94)	46	0.489	p value: 0.52218
PLHA (247)	128	51.82	z score: 0.3657
PLHA 0.71138 on cotrimoxazole (170)	85	0.50	p value: 0.71138
PLHA with metabolic syndrome (38)	15	0.39	z score: -1.6561
PLHA 0.09692 without metabolic syndrome (209)	113	0.54	p value: 0.09692

LFT, liver function tests; ART, antiretroviral therapy; ATT, anti-tubercular therapy; PLHA, people living with HIV/AIDS.

Table 4 – Grades of liver dysfunction in various groups.

	n	Abnormal LFT (128)	Grade I & II (113)	Grade III & IV (15)	z score	p value
Sex						
Female	74	34	31	3	0.612	0.54
Male	173	94	82	12	-0.612	0.54
ART	211	109	95	14	-0.948	0.34
Nevirapine	121	54	42	12	-3.156	0.0016
PIs	9	4	3	1	-0.839	0.40
ATT	111	56	46	10	-1.904	0.057
ATT-ART	94	46	36	10	-2.639	0.0083
HBsAg positive	2	2	0	2	-3.912	0.0001.

LFT, liver function tests; ART, antiretroviral therapy; ATT, anti-tubercular therapy; PIs, protease inhibitors; HBsAg, hepatitis B surface antigen.

± 169.59 cells/ μ L. Fourteen of these patients were on ART, and out of these 12 were on nevirapine-based therapy. Two patients were HBsAg positive; with one having features of chronic liver disease. One female patient was diagnosed to have autoimmune hepatitis. Severe LFT abnormalities were commoner in nevirapine group ($p = 0.02$) and in combined ART-ATT group (p value = 0.008). Table 4 summarizes the grades of liver function abnormalities in various subgroups.

The mean albumin globulin ratio (AG ratio) was 1.2173 ± 0.385 and 1.1019 ± 0.469 in normal and abnormal LFT group respectively and the difference was significant ($p = 0.037$). There was positive co-relation between AG ratio and CD4 count (0.241; $p = 0.0002$); however there was no significant co-relation between AG ratio and duration of HIV infection (0.039; $p = 0.542$).

Discussion

The aim of this study was to determine the prevalence of liver function abnormalities in PLHA. The prevalence of LFT abnormalities in our HIV population was 51.82% as has been documented in other studies among HIV-infected persons.^{23–25} Though more than 50% of our patients had LFT abnormalities, only 11.72% had severe abnormalities of liver function (grade III & IV). LFT abnormalities were similar in HIV patients irrespective of them being on ART, ATT, or on concurrent ATT-ART or those who consumed significant amounts of alcohol. Severe LFT abnormalities were commoner in those on nevirapine and those receiving concurrent ATT-ART.

Nevirapine is considered to be the most hepatotoxic of all ART drugs. In our study LFT abnormalities were commoner in the non-nevirapine group ($p = 0.043$). This may be due to the fact that nevirapine is known to cause liver toxicity when given to individuals who have higher CD4 count (>350 cells/dL)²⁶ whereas mean CD4 count in our cohort was 350.065 ± 328.475 /dL. The latest guidelines for management of HIV infection recommend starting ART in HIV-positive persons with CD4 count ≥ 350 cells/dL.^{27,28} As ART will now be initiated at higher basal CD4 cell count levels, the incidence of nevirapine-related hepatotoxicity can be expected to rise. The other group where nevirapine is notorious to cause liver toxicity is pregnant women with high CD4 count; we did not have any pregnant patient in our cohort. In patients being put on ATT, efavirenz was used instead of nevirapine to avoid hepatotoxicity. Severe LFT abnormalities were however more prevalent in nevirapine group ($p = 0.02$) and in combined ATT-ART group ($p = 0.008$). In patients with severe LFT abnormalities, nine patients on concurrent ATT-ART were being administered nevirapine based therapy; which might explain the higher rise in transaminases. Drug induced liver toxicity is also commonly associated with protease inhibitors²⁹; however, in our study, very few patients were on protease inhibitors.

Significant alcohol consumption was seen in 28.34% of the persons who were studied. Deranged LFT was not higher in this group as compared with the rest of the cohort. We found a very low prevalence of HBV and HCV infection in our patients with HIV (HBV-2, HCV-1). Worldwide, the prevalence of HBV

and HCV infection in HIV-infected patients is documented to be around 80–90%^{1–3} and 30%^{14,15,30} respectively whereas in India, it has been reported between 2.25–29.7%³¹ and 1.3–8.3%^{17–19,32} respectively. In intra-venous drug users, the prevalence of HCV in PLHA has been documented to be between 13.2% and 86% in India.^{33–36} The reason for this low prevalence of HBV infection in our study can be that, we did not test for IgG anti-HBc antibody nor did we look for HBV DNA. Studies have shown a positive rate of HBV DNA of 10% in patients who were HBsAg negative but tested positive for anti-HBc IgG antibodies.³⁷ We had only one patient who was Anti HCV positive. As per another study done in our centre (unpublished data); the prevalence of Anti HCV antibody in PLHA is 0.39% (8/2020). There were no IV drug users (IVDUs) or men who had sex with men (MSM) in our study population and this may account for the lower prevalence of HCV. The other reason for low prevalence of HCV infection in our cohort is that we only tested for antibody response to HCV infection which may be blunted in immunocompromised state like HIV infection.^{38,39} A more definite way of documenting HCV infection in immunocompromised state would have been testing for HCV RNA.

Another important observation was the significant correlation between AG ratio and CD4 count (0.241; *p* value: 0.0002). Also the AG ratio was higher in the subgroup with normal LFT as compared to that with abnormal LFT (1.2173 ± 0.385 vs 1.1019 ± 0.469 ; *p* value: 0.037). With lower CD4 cell counts, patients are more likely to have other opportunistic infections and this may account for lower serum albumin levels (negative acute phase reactant). It was further observed, that patients with active tuberculosis (on ATT) had lower AG ratio (0.934 ± 0.32). Hence all patients of HIV with lower AG ratio should be actively screened for opportunistic infections, especially tuberculosis.

To summarize, LFT abnormalities in PLHA are quite common; however, majority of them have only mild dysfunction (88.28%). While there was no statistically significant difference in LFT abnormalities in ART, ATT or ATT-ART groups; severe abnormalities in LFT were significantly commoner in those patients on nevirapine-based therapy and in those on concurrent ATT-ART. The prevalence of HBV and HCV co-infections in our cohort was very low.

Conflicts of interest

The authors have none to declare.

REFERENCES

- Dieterich DT, Robinson PA, Love J, Stern JO. Drug-induced liver injury associated with the use of nonnucleoside reverse-transcriptase inhibitors. *Clin Infect Dis*. 2004;38(suppl 2):S8.
- Wnuk AM. Liver damage in HIV-infected patients. *Med Sci Monit*. 2001;7:729–736.
- Palella Jr FJ, Baker RK, Moorman AC, et al. Mortality in the highly active antiretroviral therapy era: changing causes of death and disease in the HIV outpatient study. *J Acquir Immune Defic Syndr*. 2006;43(1):27–34.
- Bica I, McGovern B, Dhar R, et al. Increasing mortality due to end-stage liver disease in patients with human immunodeficiency virus infection. *Clin Infect Dis*. 2001;32(3):492–497.
- Martin-Carbonero L, Soriano V, Valencia E, Garcia-Samaniego J, Lopez M, Gonzalez-Lahoz J. Increasing impact of chronic viral hepatitis on hospital admissions and mortality among HIV-infected patients. *AIDS Res Hum Retroviruses*. 2001;17(16):1467–1471.
- Weber R, Sabin CA, Friis-Møller N, et al. Liver-related deaths in persons infected with the human immunodeficiency virus: the D:A:D study. *Arch Intern Med*. 2006;166(15):1632–1641.
- Sulkowski MS. Management of hepatic complications in HIV-infected persons. *J Infect Dis*. 2008;197(suppl 3):S279–S293.
- Chaudhry AA, Sulkowski MS, Chander G, Moore RD. Hazardous drinking is associated with an elevated aspartate aminotransferase to platelet ratio index in an urban HIV-infected clinical cohort. *HIV Med*. 2009;10:133–142.
- Guarda LA, Luna MA, Smith Jr JL, Mansell PW, Gyorkey F, Roca AN. Acquired immunodeficiency syndrome: postmortem findings. *Am J Clin Pathol*. 1984;81:549–557.
- Price JC, Thio CL. Liver disease in the HIV-infected individual. *Clin Gastroenterol Hepatol*. 2010;8:1002–1012.
- Gordon SC, Reddy KR, Gould EE, et al. The spectrum of liver disease in the acquired immunodeficiency syndrome. *J Hepatol*. 1986;2:475–484.
- Francisci D, Baldelli F, Papili R, Stagni G, Pauluzzi S. Prevalence of HBV, HCV, HDV markers in HIV-positive patients. *Eur J Epidemiol*. 1995;11:123–126.
- Lebovics E, Dworkin BM, Heier SK, Rosenthal WS. The hepatobiliary manifestations of human immunodeficiency virus infection. *Am J Gastroenterol*. 1988;83:1–7.
- Alberti A, Clumeck N, Collins S, et al. Short statement of the first European consensus conference on the treatment of chronic hepatitis B and C in HIV-coinfected patients. *J Hepatol*. 2005;42:615–624.
- Cotler SJ, Jensen DM. Treatment of hepatitis C virus and HIV coinfections. *Clin Liver Dis*. 2001;5:1045–1061.
- Thomas DL. Hepatitis C and human immunodeficiency virus infection. *Hepatology*. 2002;36(5 suppl 1):S201–S209.
- Puri P, Anand AC, Saraswat VA, et al. Consensus Statement of HCV Task force of the Indian National Association for Study of the Liver (INASL). Part I: status report of HCV infection in India. *J Clin Exp Hepatol*. 2014;4:104–114.
- Nagmoti MB, Patil CS, Jyoti MN, Mutnal MB, Mallapur MD. Prevalence of hepatitis C infection in HIV-seropositive individuals in and around Belgaum, south India. *Int J STD AIDS*. 2012;23(October (10)):e14–e15.
- Sonth SB, Satyhanarayana MS, Mariraj J, Krishna S. Sero-prevalence of anti-HCV in HIV infected patients. *J Commun Dis*. 2011;43(2):151–154.
- Schneider MF, Gange SJ, Williams CM, Anastos K, Greenblatt RM, Kingsley L. Patterns of the hazard of death after AIDS through the evolution of antiretroviral therapy: 1984–2004. *AIDS*. 2005;19(17):2009–2018.
- Palella Jr FJ, Delaney KM, Moorman AC, et al. Declining morbidity and mortality among patients with advanced human immunodeficiency virus infection, HIV Outpatient Study Investigators. *N Engl J Med*. 1998;338(13):853–860.
- AIDS Clinical Trial Group. *Table of Grading Severity of Adult Adverse Experiences*. Rockville MD: Division of AIDS, National Institute Of Allergy and Infectious Diseases; 1996.
- Ioannou GN, Boyko EJ, Lee SP. The prevalence and predictors of elevated serum aminotransferase activity in the United States in 1999–2002. *Am J Gastroenterol*. 2006;101:76–82.

24. Pol S, Lebray P, Vallet-Pichard A. HIV infection and hepatic enzyme abnormalities: intricacies of the pathogenic mechanisms. *Clin Infect Dis*. 2004;38:S65–S72.
25. Sterling RK, Chiu S, Snider K, Nixon D. The prevalence and risk factors for abnormal liver enzymes in HIV-positive patients without hepatitis B or C coinfections. *Dig Dis Sci*. 2008;53:1375–1382.
26. Shubber Z, Calmy A, Andrieux-Meyer I, et al. Adverse events associated with nevirapine and efavirenz-based first-line antiretroviral therapy: a systematic review and meta-analysis. *AIDS*. 2013;27:1403–1412.
27. WHO Early Release Guidelines on When to Start Antiretroviral Therapy and on Pre-exposure Prophylaxis for HIV. 2015, September. Available from: <http://www.who.int/hiv/pub/guidelines/early-release-arv/en/> [accessed 10.04.16].
28. European AIDS Clinical Society Guidelines, Version 8.0. 2015, October. Available from: <http://www.eacsociety.org/guidelines/eacs-guidelines/eacs-guidelines.html> [accessed 10.04.16].
29. Nunez M. Clinical syndromes and consequences of antiretroviral related hepatotoxicity. *Hepatology*. 2010;52:1143–1155.
30. Thomas DL. Hepatitis, C and human immunodeficiency virus infection. *Hepatology*. 2002;36(5 suppl 1):S201–S209.
31. Puri P. Tackling the hepatitis B disease burden in India. *J Clin Exp Hepatol*. 2014;4:312–319.
32. Chandra N, Joshi N, Raju YS, Kumar A, Teja VD. Hepatitis B and/or C co-infection in HIV infected patients: a study in a tertiary care centre from South India. *Indian J Med Res*. 2013;138(6):950–954.
33. Solomon SS, Mehta SH, Srikrishnan AK, Solomon S, McFall AM, Laeyendecker O. Burden of hepatitis C virus disease and access to hepatitis C virus services in people who inject drugs in India: a cross-sectional study. *Lancet Infect Dis*. 2015;15(1):36–45.
34. Ray Saraswati L, Sama A, Sebastian MP, et al. HIV, Hepatitis B and C among people who inject drugs: high prevalence of HIV and Hepatitis C RNA positive infections observed in Delhi, India. *BMC Public Health*. 2015;15:726.
35. Devi KS, Singh NB, Singh HL, Singh YM. Coinfection by human immunodeficiency virus, hepatitis B virus and hepatitis C virus in injecting drug users. *J Indian Med Assoc*. 2009;107(3). 144, 146–147.
36. Solomon SS, Srikrishnan AK, Mehta SH, et al. High prevalence of HIV, HIV/hepatitis C virus coinfection, and risk behaviors among injection drug users in Chennai, India: a cause for concern. *J Acquir Immune Defic Syndr*. 2008;49(3):327–332.
37. Gandhi RT, Wurcel A, Lee H, et al. Isolated antibody to hepatitis B core antigen in human immunodeficiency virus type-1-infected individuals. *Clin Infect Dis*. 2003;36:1602.
38. Bonacinin M, Liu HJ, Hollinger FB. Effect of co-existing HIV-1 infection on the diagnosis and evaluation of hepatitis C virus. *J AIDS*. 2001;26:340–344.
39. Mohsen AH, Easterbrook P, Taylor CB, Norris S. Hepatitis C and HIV-1 co infection. *Gut*. 2002;51:601–608.

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