Published in final edited form as:

J Acquir Immune Defic Syndr. 2008 October 1; 49(2): 233–234. doi:10.1097/QAI.0b013e31816de85f.

UNCOMMON HBV AND/OR HCV OCCULT INFECTION IN HIV-POSITIVE PATIENTS with ABNORMAL LEVEL OF HEPATIC ENZYME

Natalia Laufer, Lucila Cassino, Federico Bolcic, Franco Moretti, Rita Reynoso, Maria Belen Bouzas, Pedro Cahn, Horacio Salomón, and Jorge Quarleri

To the editor

Elevated liver enzyme levels, detected through liver function test (LFT), are markers of liver or biliary tract diseases. Alanine aminotransferase (ALT) is a more specific indicator of liver inflammation. These abnormal findings are very frequent in HIV infected patients and their diagnosis and management may be difficult because of intricacies of the pathogenic mechanism involved¹. Recently Sterling et al. evaluated the prevalence and factors associated with abnormal LFTs, particularly focusing in patients without viral hepatitis coinfection. They reported a higher prevalence of elevated LFTs in HIV-positive patients without HCV/HBV infection (15-20%) than in general population (8%)². Increased ALT was associated in this study with hypertension, HIV viral load, LT- CD4 count lower than 200 cells/ml, metabolic syndrome and absence of proteases inhibitors use. They did not study the presence of occult HCV and/or HBV infection in those patients with negative serology².

During a seven-month period (September 2004 to March 2005) all HIV positive patients ≥ 18 years old follow-up at a General Hospital in Buenos Aires that have their scheduled control of HIV viral load (VL) at the National Reference Centre for AIDS were asked to consent for the use of their serum samples to evaluate HBV and HCV serology status and ALT level. Only the first blood sample of patients with more than one control of HIV VL during this period was included. Diagnostic procedures included: HCV Ab (MEIA and HCV 3.0 Murex), HBV: HBsAg, HBsAb, HBeAg, HBeAb and HBeAb (IgM and total) by MEIA (AXSYM Abbott). ALT levels were determined by Biosystem (normal value 41UI/ml). The presence of HCV RNA was determined for all samples proven to be reactive in any of the serological tests or with abnormal LFTs. Two different RT-PCR qualitative approaches were used: an in-house assay previously described³ and a commercial one (AMPLICOR HCV test kit, version 2.0, lower detection level 50 IU/mL, Roche Molecular Systems). Specimens containing detectable HCV RNA were genotyped by using the restriction fragment length polymorphism (RFLP) method previously described³.

For quantitative purposes, a commercial assay (Bayer VERSANT® HCV RNA 3.0 Assay – bDNA- test kit; ranging from 615 to 7,700,000 HCV RNA IU/mL) was carried out.

The presence of HBV DNA was studied by polymerase chain reaction (PCR) reaching an amplicon (585 nt, from nucleotide 203 to 787) of the HBV surface (S) gene, as described by Zeng et al⁴. The HBV genotype was determined by phylogenetic analysis of the above PCR product corresponding to S gene partial sequence. For this purpose, the amplification products were sequenced directly on both strands, using the BigDye Terminator Cycle Sequencing Ready Reaction Kit on an ABI PRISM 3100 Genetic Analyzer (Applied Biosystems, Foster City, CA).

A total of 593 consecutive patients were included. Overall 41.6% (246) had markers of HBV infection and 20% (129) did so for HCV, 65 cases (11%) showed markers for both. Abnormal LFTs were found in 104 (17.5%) of the samples: 77 (74%) between one to two times over the normal upper limit (grade 0-1 according to NIH-NIAID⁵), and 27 (26%) more than two times (grade 2). Clinical records review and in 75% of them persistent abnormal ALT was observed (i.e.: presented 2 out of 3 determinations above the normal level during a 12 months period⁶). Among those with abnormal LFTs 58 (56%) showed serological markers for HBV (9 chronic carriers, 27 with “isolated core” pattern y 22 with positive HBc and HBs Ab); and 54 (52%) positive HCV serology (45 with detectable HCV ARN). Thirty-one patients presented triple infection (HCV/HBV/HIV). Twenty-three patients (22%) presented negative HBV and HCV serology. (Figure 1)

Among patients with serological markers of HBV infection, 9 had positive HBsAg with positive HBeAg in 8 of them, and a median of HBV VL of 5.200.000 copies/mL (range < 1000- >40000000), all presented ALT grade 0-1. Of the 27 samples with isolated core pattern HBV DNA was found in one of them and after sequenced no mutations were found. None of the samples with detectable HBc and HBs antibody showed positive HBV DNA. In the 23 samples with negative serology results for both HBV/HCV coinfections, the presence of HCV RNA and HBV DNA was investigated. None of the samples exhibited HCV ARN and only one showed positive HBV DNA.

Abnormal ALT was more frequent in the group of intravenous drugs users; probably related with the higher risk of hepatitis coinfection in this population.

Among the patients in whom their antiretroviral scheme was known (n=81/104) 75% were receiving NNRTI, and in 69% absence of IP use was recorded, in concordance with the results of Sterling².

Despite we could not found a statistically significant association between elevated ALT and CD4 count but we can estimate that it was a trend to have a lower CD4 count among patients with this abnormality (328 vs. 383 cell/mL, p 0.055).

Our data shows that most of the cases abnormal ALT in our population are generally mild and are associated with active HBV/HCV infection, being the majority of them detectable with serology assays. Considering the results of our study the routinely search of HBV DNA and/or HCV ARN in HIV-positive patients, even in the setting of elevated ALT, would not be recommended and should be implemented in a case by case basis.

References

1. Pol S, Lebray P, Vallet-Pichard A. HIV infection and hepatic enzyme abnormalities: intricacies of the pathogenic mechanisms. Clin Infect Dis 2004;38:S65–72. [PubMed: 14986277]
2. 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. 2007;10.1007/s10620-007-9999-6
2. Amrstrong GL, Wasley A, Simard EP, et al. The prevalence of hepatitis C virus infection in the United States, 1999–2002. Ann Intern Med 2006;144:705–714. [PubMed: 16702586]
3. Quarleri JF, Robertson BH, Mathet VL, et al. Genomic and phylogenetic analysis of Hepatitis C virus isolates from Argentine patients: a 6 yr-retrospective study. R J Clin Microbiol 2000;38:4560–4568.
4. Zeng GB, Wen SJ, Wang ZH, Yan L, Sun J, Hou JL. A novel hepatitis B virus genotyping system by using restriction fragment length polymorphism patterns of S gene amplicons. World J Gastroenterol 2004;10(21):3132–6. [PubMed: 15457558]
5. ACTG Clinical Group. Division of AIDS table for grading the severity of adult and pediatric adverse events. NIH-NIAID; 2004.

6. Soriano V, Puoti M, Sulkowski M, et al. Care of patients coinfectd with HIV and hepatitis C virus: 2007 updated recommendations from the HCV-HIV International Panel. *AIDS* 2007;21:1073–89. [PubMed: 17502718]

Figure 1.

HBsAg : HBV surface antigen, HBcAB: HBV core antibody, HBsAb+: HBV surface antigen, Isolated HBcAb: HBcAb+/HBsAg and HBsAb NEG. HBV DNA +: positive PCR for HBV deoxyribonucleic acid; HCV ARN+: positive PCR for HCV ribonucleic acid.