IOSR Journal of Pharmacy and Biological Sciences (IOSR-JPBS)
e-ISSN: 2278-3008, p-ISSN:2319-7676. Volume 9, Issue 2 Ver. II (Mar-Apr. 2014), PP 24-29
www.iosrjournals.org

Transaminase [alanine aminotransferase (ALT) and aspartate aminotransferase (AST)] Activity of HIV and HBV Co-Infected Female Patients on Drugs and Female Patients Not on Drugs

ODIBA, Arome Solomon[1], UKEGBU, Chimere Young[2], OMEJE, Kingsley Ozioma[2], ONOSAKPONOMEIruoghene[2], IROHA, Okechukwu Kalu[2]
[1] *Department of Biochemistry, University of Jos, Plateau State, Nigeria*
[2] *Department of Biochemistry, University of Nigeria, Enugu State Nigeria*

Abstract: *Human immunodeficiency virus-1 (HIV) and hepatitis B virus (HBV) co-infection is a major threat, especially to liver damage. 100 female patients referred to Virology department of the Jos University teaching Hospital (JUTH), were selected by physicians on the basis of the following criteria: documented HIV infection, no alcohol abuse (≤ 20 g alcohol daily and no history of chronic alcohol consumption), no history of hereditary and autoimmune liver disease, no evidence of hemochromatosis. Data on demographics, drug or alcohol use, and history of liver diseases were obtained at first visit. A month-by-month documentation of the prescribed drug combination allowed a calculation of each patient's individual cumulative drug exposure. Subjects were then classified into control (30), co-infected; on drugs (35) and co-infected; not on drugs (35). The test for HIV antibodies, HBsAg were carried out on day one (at first visit) serum ALT and serum AST were determined three (3) months after detection (day 90; after HIV antigen confirmatory test). Thirty-five (35) patients started medication at day-one, and 35 decided not to start medication until after confirmatory test (three months later).The serum ALT levels of the HIV-HBV co-infected patients on drugs (M=43.60, SD=1.83) was significantly higher than the serum ALT levels of the control group (M=29.17, SD=6.17), t (63) =12, p< .0001 at p <.05 confidence level. In a similar trend, the serum ALT levels of the HIV-HBV co-infected patients not on drugs (M=37.74, SD=3.70) was significantly higher than the serum ALT levels of the control group (M=29.17, SD=6.17), t (63) =6.5, p< .0001 at p <.05 confidence level. On comparison, the serum ALT levels of the HIV-HBV co-infected patients on drugs (M=43.60, SD=1.83) was significantly higher than the serum ALT levels of the HIV-HBV co-infected patients not on drugs (M=37.74, SD=3.70), t (68) =8.40, p< .0001 at p <.05 confidence level. The serum AST levels of the HIV-HBV co-infected patients on drugs (M=43.54, SD=2.74) was significantly higher than the serum AST levels of the control group (M=32.23, SD=5.93), t (63) =10, p< .0001 at p <.05 confidence level. In a similar manner, the serum AST levels of the HIV-HBV co-infected patients not on drugs (M=37.66, SD=2.11) was significantly higher than the serum AST levels of the control group (M=32.23, SD=5.93), t (63) =5.1, p< .0001 at p <.05 confidence level. On comparison, the serum AST levels of the HIV-HBV co-infected patients on drugs (M=43.54, SD=2.74) was significantly higher than the serum AST levels of the HIV-HBV co-infected patients not on drugs (M=37.66, SD=2.11), t (68) =10.07, p< .0001 at p <.05 confidence level. HIV-HBV infection causes liver damage with more damage caused by drugs taken to manage these infections. A correlation analysis between ALT and AST levels shows a non-significant correlation.*

Keywords: *alanine transaminase, aspartate transaminase, drugs, female, hepatitis B virus,human immune deficiency virus*

I. Introduction

Human immunodeficiency virus-1 (HIV) and hepatitis B virus (HBV) are both transmitted through sexual and percutaneous routes [1]. There are many common infections globally, amongst which the HIV and HBV co-infection is a major threat. Worldwide, it is estimated that 10% of the 40 million HIV-infected individuals have chronic hepatitis B [2]. The prevalence of HIV-infected persons carrying hepatitis B surface antigen (HBsAg) varies according to geography and risk category, being higher among men who have sex with men and in developing countries such as Nigeria.

HBV is a DNA virus that forms stable circular covalently closed (CCC) DNA that can persist in the liver indefinitely. Individuals with core antibody positivity are at risk of HBV reactivation, particularly in the setting of severe immune-compromise, prolonged steroid use, or chemotherapy. There are 8 genotypes of HBV. Genotype G may be predictive of more severe fibrosis in HIV co-infected patients, [3] and genotypes C and D may be more responsive to interferon [4]. Nucleosides are however, the mainstays of HBV treatment. Since the introduction of highly active antiretroviral therapy (HAART) in the United States and other industrialized

countries, deaths from AIDS-related causes have declined, but liver disease has emerged as one of the leading causes of morbidity and mortality [5], [6].

Management of hepatitis B in patients infected with HIV is complicated not only by the differences in natural history but also by other issues such as the activity of several drugs against both viruses and development of drug-resistant HIV and HBV variants. The course of acute HBV may be modified in the presence of HIV infection, with a lower incidence of icteric illness and lower rates of spontaneous clearance of HBV. Persons with HIV and chronic HBV co-infection have higher levels of HBV DNA and lower rates of clearance of the hepatitis B antigen (HBeAg) [7], [8]. Serum transaminase levels may be lower in HIV/HBV co-infected patients than in HBV mono-infected patients. Liver disease has emerged as a leading cause of morbidity and mortality in HIV-infected individuals. The management of hepatitis B in HIV infection iscomplicated by the dual activity of several nucleoside analogs. HBV is 100-fold more likely to be transmitted than HIV [9]. HIV increases the risk of cirrhosis and end-stage liver disease in HBV co-infection. A transaminase is a type of enzyme whose activity is frequently measured, as part of a standard series of tests, to determine liver function. There are a number of different types of transaminases, but the two commonly measured medically are alanine transaminase (ALT) and aspartate transaminase (AST). ALT is primarily localized to the liver and is considered a more specific test for liver damage. Elevated serum transaminase levels [alanine aminotransferase (ALT) and aspartate aminotransferase (AST)] in human immunodeficiency and HBV co-infected patients is an indication of a threat to the system. Damages done on the body system as a result of infectious disease do reflect in the activities of liver transaminases. Therefore, ordering for a laboratory investigation on liver transaminases profile is a test to assess the level of damage. Liver damage is associated with chronic high serum transaminases in human immunodeficiency virus (HIV) and HBV co-infected patients under combined antiretroviral therapyhepatitis B and HIV co-infection patients portray more HBV-related liver disease than those with HBV infection alone[10]. Likewise, persons with HIV and HBV co-infection have a significant increase in liver-related mortality, compared to those who are infected with HBVonly [11]. Also, HIV-infected patients co-infected with HBV have an increased risk for antiretroviral therapy-related hepatotoxicity [12]. Patients co-infected with HIV and HBV who receive treatment for HBV and antiretroviral therapy at the same time may decrease their level of risk for antiretroviral therapy-related hepatotoxicity [13]. There are many agents used to treat hepatitis B, but the activity of these agents against HIV varies from partial activity to no activity at all. Antiretroviral agents that have strong activity against both HIV and HBV include: tenofovir, emtricitabine, and lamivudine.Most HIV treatment contains one or more HBV-active agents (e.g., lamivudine [3TC], emtricitabine [FTC], tenofovir [TDF]), and apart from their therapeutic effect, they burden the liver with the duty of metabolizing these drugs with detrimental, damaging effect on the liver. Interferon (IFN) is most effective for HBV treatment in patients with low levels of viremia and elevated transaminases, and it therefore may [14] and should not be used in the absence of combination be less useful in patients with HIV/HBV co-infection than in those with HBV alone. In co-infected patients, IFN has been associated with lower rates of HBV treatment success and increased toxicity [15]. Although entecavir initially was thought to have no anti-HIV activity, it has been demonstrated to select for the M184V mutation *(*ART with full suppression of HIV viremia. Telbivudine is a thymidine analogue that also selects for the HBV rtM204 mutation, which leads to 3TC cross-resistance, and should not be used after 3TC or FTC failure [16].

II. Patients And Methods

For this study 100 female patients referred to Virology department of the Jos University teaching Hospital (JUTH), were selected by their physicians on the basis of the following criteria: documented HIV infection, no alcohol abuse (≤ 20 g alcohol daily and no history of chronic alcohol consumption), no history of hereditary and autoimmune liver disease, no evidence of hemochromatosis. Patients with any contraindication for liver biopsy were excluded. Data on demographics, drug or alcohol use, and history of liver diseases were obtained at first visit. A month-by-month documentation of the prescribed drug combination allowed a calculation of each patient's individual cumulative drug exposure. Subjects were then classified into control (30), co-infected; not on drugs (35) and co-infected; on drugs (35). The test for HIV antibodies, HBsAg were carried out on day one (at first visit) serum ALT and serum AST were determined three (3) months after detection (day 90; after HIV antigen confirmatory test). Thirty-five (35) patients started medication at day one and 35 decided not to start medication until after confirmatory test (three months later). Both the HIV antibodies, HBsAg assessment was carried out using Fortress HIV 1&2 STRIP and Fortress HbsAg ELISA test kit respectively. Serum ALT and serum AST were carried out spectrophotometrically.

2.1 Parameters

The biochemical parameters for laboratory assessment included HIV antibodies, HBsAg, serum ALT and serum AST.

2.2 Statistical analysis.

Variables with a normal distribution were expressed as mean and standard deviation as well as comparison using T test all measured variables were considered in analysis and also a correlation analysis between the ALT and AST. Analyses were performed using IBM SPSS package version 20.

III. Results

Table 1: ALT andAST levels of control group [HIV (-ve), HBV(-ve)]

S/N of patients	HIV Status	HBV Status	ALT (Iu/L)	AST/ (Iu/L)
01	-	-	38	38
02	-	-	37	37
03	-	-	40	40
04	-	-	22	36
05	-	-	19	37
06	-	-	17	36
07	-	-	33	36
08	-	-	24	24
09	-	-	23	26
010	-	-	22	33
011	-	-	27	37
012	-	-	36	40
013	-	-	37	39
014	-	-	36	18
015	-	-	36	22
016	-	-	26	34
017	-	-	31	33
018	-	-	34	33
019	-	-	25	24
020	-	-	24	24
021	-	-	26	35
022	-	-	23	39
023	-	-	33	29
024	-	-	33	26
025	-	-	40	37
026	-	-	22	34
027	-	-	23	28
028	-	-	31	30
029	-	-	33	30
030	-	-	24	32

Table 2: ALT andAST levels of HIV (+ve), and HBV (+ve) patients on drugs

S/N of patients	HIV Status	HBV Status	ALT (Iu/L)	AST (Iu /L)
031	+	+	43	43
032	+	+	44	42
033	+	+	43	43
034	+	+	44	43
035	+	+	44	43
036	+	+	43	44
037	+	+	43	46
038	+	+	43	46
039	+	+	42	49
040	+	+	42	48
041	+	+	45	42
042	+	+	44	40
043	+	+	45	41
044	+	+	42	41
045	+	+	44	41
046	+	+	43	44
047	+	+	43	44
048	+	+	44	45
049	+	+	42	47
050	+	+	47	43
051	+	+	41	42
052	+	+	48	49
053	+	+	49	49
054	+	+	39	40
055	+	+	44	38
056	+	+	44	42
057	+	+	43	43

058	+	+	45	42
059	+	+	43	43
060	+	+	43	43
061	+	+	43	43
062	+	+	42	44
063	+	+	44	48
064	+	+	45	41
065	+	+	43	42

Table 2: ALT andAST levels of HIV (+ve), and HBV (+ve) patients not on drugs

S/N of patients	HIV Status	HBV Status	ALT (Iu/L)	AST (Iu /L)
066	+	+	38	39
067	+	+	40	40
068	+	+	40	38
069	+	+	39	39
070	+	+	39	38
071	+	+	39	37
072	+	+	38	40
073	+	+	40	36
074	+	+	32	37
075	+	+	32	36
076	+	+	35	36
077	+	+	37	38
078	+	+	42	37
079	+	+	49	40
080	+	+	38	36
081	+	+	38	37
082	+	+	38	36
083	+	+	39	36
084	+	+	36	39
085	+	+	47	40
086	+	+	37	40
087	+	+	35	38
088	+	+	36	38
089	+	+	39	33
090	+	+	40	40
091	+	+	38	39
092	+	+	38	39
093	+	+	33	35
094	+	+	33	34
095	+	+	34	39
096	+	+	32	39
097	+	+	35	40
098	+	+	35	41
099	+	+	40	33
100	+	+	40	35

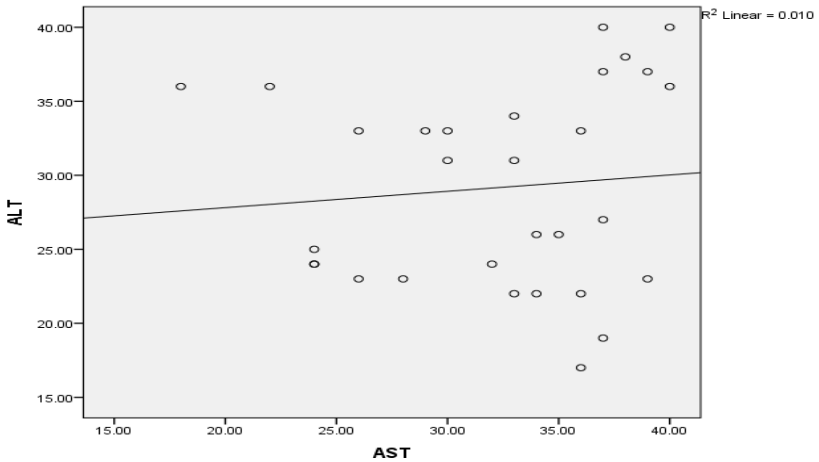

Figure 1: a correlation plot between ALT and AST levels of the control group

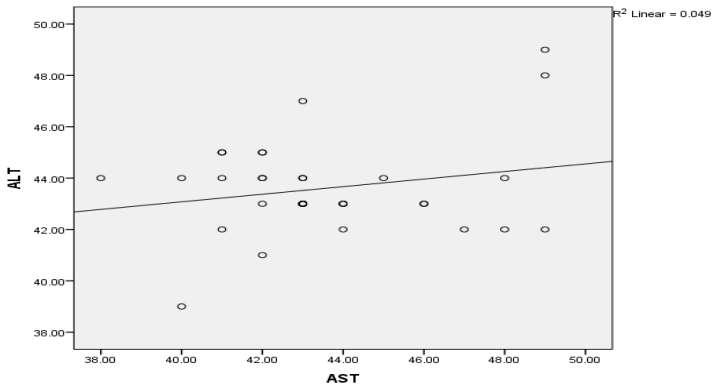

Figure 2: a correlation plot between ALT and AST levels of HIV (+ve), and HBV (+ve) patients on drugs

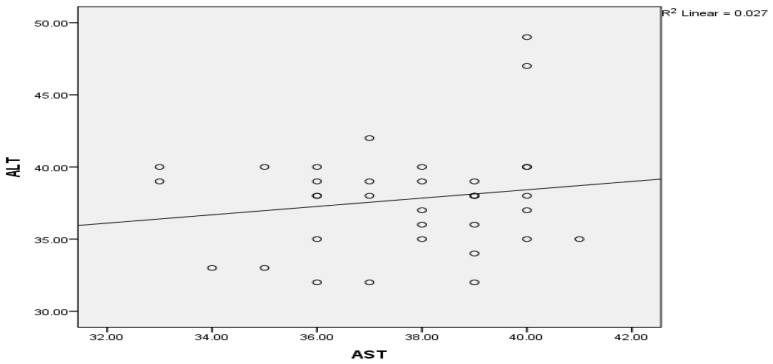

Figure 3: a correlation plot between ALT and AST levels of HIV (+ve), and HBV (+ve) patients not on drugs

IV. Discussion

The serum ALT levels of the HIV-HBV co-infected patients on drugs (M=43.60, SD=1.83) was significantly higher than the serum ALT levels of the control group (M=29.17, SD=6.17), t (63) =12, p< .0001 at p <.05 confidence level. In a similar trend, the serum ALT levels of the HIV-HBV co-infected patients not on drugs (M=37.74, SD=3.70) was significantly higher than the serum ALT levels of the control group (M=29.17, SD=6.17), t (63) =6.5, p< .0001 at p <.05 confidence level. On comparison, the serum ALT levels of the HIV-HBV co-infected patients on drugs (M=43.60, SD=1.83) was significantly higher than the serum ALT levels of the HIV-HBV co-infected patients not on drugs (M=37.74, SD=3.70), t (68) =8.40, p< .0001 at p <.05 confidence level.

The serum AST levels of the HIV-HBV co-infected patients on drugs (M=43.54, SD=2.74) was significantly higher than the serum AST levels of the control group (M=32.23, SD=5.93), t (63) =10, p< .0001 at p <.05 confidence level. In a similar manner, the serum AST levels of the HIV-HBV co-infected patients not on drugs (M=37.66, SD=2.11) was significantly higher than the serum AST levels of the control group (M=32.23, SD=5.93), t (63) =5.1, p< .0001 at p <.05 confidence level. On comparison, the serum AST levels of the HIV-HBV co-infected patients on drugs (M=43.54, SD=2.74) was significantly higher than the serum AST levels of the HIV-HBV co-infected patients not on drugs (M=37.66, SD=2.11), t (68) =10.07, p< .0001 at p <.05 confidence level.

From the forgoing, flares in serum ALT and AST could result from many factors, which could be a direct extrapolation of the damaging effect. In patients with chronic HBV-infection who experience HBV suppression while receiving ART, flares have been reported following the discontinuation of lamivudine [17], emtricitabine [18], or tenofovir [19] treatment or with the emergence of lamivudine resistance [9].For patients co-infected with HIV-HBV, a higher flare in has been reported when they start receiving combination antiretroviral therapy, and the flares may be attributed to drug related hepatotoxicity [19].A very common cause of late flares during combination antiretroviral therapy is the emergence of HBV strains that are resistant to lamivudine, which are marked by an increase in HBV DNA and the appearance of the YMDD mutation. Also flares have been recorded after the cessation of with lamivudine, emtricitabine, adefovir, or tenofovir [17], [20], [21]. It has been observed from the study that a significant elevation of liver transaminase levels (ALT and AST) is a serious risk factor associated with management of HIV-HBV management with drugs. This is a reasonable explanation of the liver damaging potential of drugs use in the management of HIV and HBV co-infection. A correlation plot between ALT and AST levels showed a non-significant correlation between these

transaminases in the three groups. Control group (r = 0.098, p<0.05), HIV (+ve), and HBV (+ve) patients on drugs (r = 0.220, p< 0.05), HIV (+ve), and HBV (+ve) patients not on drugs (r = 1.65, p< 0.05). This shows that it's not a must that errors will occur in processes that has to do with the both enzymes. This explains the fact that they both have similar but independent metabolic routes.

V. Conclusion

Markers of HBV exposure are present in a high proportion of HIV-infected individuals. HIV affects HBV viral replication and clearance, accelerates the development of liver disease, and contributes significantly to hepatic morbidity and mortality in HIV infection. HBV coinfection does not appear to influence the rate of HIV progression but may be a surrogate for factors associated with HIV seroconversion. Patients receiving HIV treatment should receive fully active HBV treatment as well, avoiding 3TC or FTC monotherapy. Conversely, it is preferred to give fully active ART in conjunction with HBV therapy, as there are limited options for effective HBV treatment that lack anti-HIV activity. HIV-HBV infection causes liver damage with more damage caused by drugs taken to manage these infections. Other factors may also cause the levels of these aminotransferases to elevate. Therefore, such other factors should be investigated alongside HIV-HBV co-infection investigation. It is paramount to know that drugs with minimal damaging effect on the liver, yet effective, should be used to manage such patients.

Acknowledgements

We wish to sincerely appreciate the virology department of the Jos University Teaching Hospital (JUTH) for making their patients as well as equipment available for this study.

References

[1] B. H. McGovern, The epidemiology, natural history and prevention of hepatitis B: implications of HIV co-infection, *Antiviral Therapy, 12*, 2007, H3-H13.
[2] M. J. Alter, Epidemiology of viral hepatitis and HIV co-infection, *Journal of Hepatology, 44*, 2006, S6-S9.
[3] K. Lacombe, V. *Massari*, P. M. *Girard, Major role of hepatitis B genotypes in liver fibrosis during coin*fection with HIV. AIDS, *20(3)*, 2006, *419-427.*
[4] N. *Akuta*, H. *Kumada, Influence of hepatitis B virus genotypes on the* response to antiviral therapies, *Journal of Antimicrobial Chemotherapy, 55(2), 2005,139-142.*
[5] F. J. Palella, R. K. Baker, A. C. Moorman, J. S. Chmiel, K. C. Wood, J. T. Brooks, mortality in the highly active antiretroviral therapy era: changing causes of death and disease in the HIV outpatient study, *Journal of Acquired Immune Deficiency Syndrome,43*, 2006, 27-34.
[6] C. Lewden, D. Salmon, P. Morlat, S. Bevilacqua, E. Jougla, F. Bonnet, Causes of death among human immunodeficiency virus (HIV) - infected adults in the era of potent antiretroviral therapy: emerging role of hepatitis and cancers, persistent role of AIDS, *International Journal of Epidemiology,34*, 2005, 121-130.
[7] C. L. *Thio, Hepatitis B in the human immunodeficiency virus-infected patient: epidemiology*, natural history, and treatment, *Seminars on Liver Disease, 23(2)*, 2003, 125-1*36.*
[8] L. *Piroth*, D. *Sène*, S. *Pol*, *Epidemiology, diagnosis and treatment of chronic hepatitis B in HIV-infected patients (EPIB 2005 STUDY). AIDS, 21(10),* 2007, *1323-3131.*
[9] L. E. Chapman, E.E. Sullivent, L. A. Grohskopf, E. M. Beltrami, J. F. Perz, K. Kretsinger, Recommendations for postexposure interventions to prevent infection with hepatitis B virus, hepatitis C virus, or human immunodeficiency virus, and tetanus in persons wounded during bombings and other mass-casualty events–United States, 2008: recommendations of the Centers for Disease Control and Prevention (CDC), *MMWR Recommendations and Reports57(RR-6),* 2008, 1-21.
[10] M. Puoti, C. Torti, R. Bruno, G. Filice, G. Carosi, Natural history of chronic hepatitis B in co-infected patients, *Journal of Hepatology, 44*, 2006, S65-70.
[11] C. L. Thio, E. C. Seaberg, R. Skolasky, HIV-1, hepatitis B virus, and risk of liver-related mortality in the Multicenter Cohort Study (MACS), *Lancet, 360,* 2002, 1921-1926.
[12] M. Savès, S. Vandentorren, V. Daucourt, Severe hepatic cytolysis: incidence and risk factors in patients treated by antiretroviral combinations. Aquitaine Cohort, France, 1996-1998. Groupe dEpidémiologie Clinique de Sida en Aquitaine (GECSA), *AIDS, 13(17),* 1999, F115-121.
[13] J. E. Kaplan, C. Benson, K. K. Holmes, Guidelines for prevention and treatment of opportunistic infections in HIV-infected adults and adolescents: recommendations from CDC, the National Institutes of Health, and the HIV Medicine Association of the Infectious Diseases Society of America, *MMWR Recommendations and Reports, 58(RR-4)*, 2009, 1-207.
[14] M. A. *McMahon*, B. L. *Jilek*, T. P. *Brennan, The HBV drug entecavir--effects on HIV-1 replication and resis*tance, *New English Journal of Medicine, 356(25)*, 2007, *2614-26*21.
[15] V. Di Martino, T. *Thevenot*, J. F. *Colin, Influence of HIV infection on the response to interferon therapy and the long-term outcome of* chronic hepatitis B, *Gastroenterology, 123(6)* 2002, *1812-18*22.
[16] E. Low, A. *Cox*, M. *Atkins, Telbivudine has activity against HIV. In: Program and abstracts of the 16th Conference on Retrovirus*es and Opportunistic Infections, February 8-11, 2009, *Montreal, Abstract 813a.*
[17] M. Bessesen, D. Ives, L. Condreay, S. Lawrence, K. Sherman, Chronic active hepatitis B exacerbations in human immunodeficiency virus– infected patients following development of resistance, *Clinical Infectious Diseases, 28*, 1999, 1032–1035.
[18] E. Mondou, J. Sorbel, J. Anderson, H. Mommeja-Marin, A. Rigney, F. Rousseau, Posttreatment exacerbation of hepatitis B virus (HBV) infection in long-term HBV trials of emtricitabine, *Clinical Infectious Diseases, 41*, 2005, e45–47.
[19] V. Soriano, J. Miro, J. Garcia-Samaniego, Consensus conference on chronic viral hepatitis and HIV infection: updated Spanish recommendations, *Journal of Viral Hepatology, 11*, 2004, 2–17
[20] Gilead Pharmaceuticals. Adefovir full prescribing information. Available at: *http:// www.gilead.com,* Accessed 20 April 2006.
[21] Gilead Pharmaceuticals. Tenofovir full prescribing information. Available at: *http:// www.gilead.com,* Accessed 20 April 2006.