

Research Article

The Prevalence Rate of Human Immunodeficiency Virus Co-infection in HBV and HCV Positive Patients in Lorestan Province: A Single Referral Center Experience

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ABSTRACT

The aim of present study was to determine the prevalence rate of Human Immunodeficiency Virus (HIV) co-infection in HBV and HCV positive patients. It was also done in order to determine the risk factors of HBV and HCV transmission in Lorestan province. In this cross-sectional study (September 2014 to September of 2016), after presenting full details to patients, their written consent was obtained, and at the next stage, they were referred to high-risk behavior counseling centers in the city. The centers tried to collect demographic and epidemiological information and to determine possible ways of transmission for each patient. Then, the patients were referred to the pathobiology labs throughout the city to conduct laboratory supplementary studies. Finally, the obtained findings were analyzed using SPSS software and $P < 0.05$ was set as the significant level of differences. Out of a total of 373 patients in this study, 252 of them (67.56%) were male and 121 (32.44%) were female. In this research, 80.7% of patients (301 patients) were suffering from HBV, 15% (56 patients) from HCV, and 4.3% (16 patients) from HBV/HCV co-infection. In this survey, all the patients were examined regarding HIV infection. The conducted tests indicated that there was no patient with HBV/HIV co-infection. On the other hand, in HCV positive patients, 9 patients (16.07 percent) were concurrently infected with HIV; in addition, of 16 patients with HBV/HCV co-infection, one patient (6.25 percent) was infected by HIV. In terms of risk factors of HBV transmission, it was observed that the most common risk factor was positive family history (37.85%), and in those with HCV infection, a history of IV drug abuse (36.11%) was the most common risk factor. Taking into consideration the risk factors for HBV and HCV infections, education about their transmission routes and prevention are emphasized.

Keywords: Hepatitis B virus, Hepatitis C virus, HIV, Co infection, Risk factors

1. INTRODUCTION

Today, catching infections of HIV, HBV, and HCV is considered as one of most important health problems of the world. Statistics are indicative that today (2014), approximately 2 billion people have been infected worldwide and

240 million are chronic carriers of HBV [1]. In Iran, prevalence rate of hepatitis B in the general population has been estimated to be about 2.2 percent based on a study carried out by Salehi-Vaziri et al in 2016, although the prevalence of the

disease has been declined due to conduction of vaccination in the recent years [2].

About 170 million people worldwide have hepatitis C that is about 3 percent of the world's population [3]. Currently, this infection is the most common cause of advanced and malignant hepatic disease in many countries [4, 5]. The prevalence of HCV infection in Iran is estimated to be 5 to 12 percent based on conducted studies, in the other word, about 200-300 thousand of people are infected by HCV in Iran [6]. Now, the main way of transmitting hepatitis C is intravenous (IV) drug addiction in developing countries [7]. The most common genotypes of hepatitis C virus is different in various parts of the world, the difference is because of many factors. However, according to the different studies conducted in various regions of Iran, the genotypes of 3a and 1a are the most common genotypes [8-10]. Worldwide, 34 million people are infected with HIV. In addition, 14 thousand people are added to this rate everyday who are mostly in developing countries [11]. HCV and HBV infections have common source of transmission with HIV infection, among which intravenous injection of drugs is the most important one [12, 13]. The conjunction of these viral causes has accelerated chronic hepatic disease and has speeded up progress to cirrhosis and hepatic cancer [14]. In some studies, simultaneous prevalence of HIV and HCV infections, in blood donors has been reported to be 0.02 [15]. On the other hand, prevalence of HIV in positive HCV patients has been estimated as 8.4 percent in the studies conducted in United States [16].

In addition to HCV/HIV co-infection, patients with HBV/HIV co-infection also are increasing [14]. In available studies, co-infection of HBV in patients with HIV has been reported as about 6.4 to 8% [13, 17]. Recent evidence has shown that HBV is significantly involved in increasing morbidity and mortality in HIV-positive patients [13]. The results of various studies indicate that the rate of HIV / HBV and HCV / HIV co-

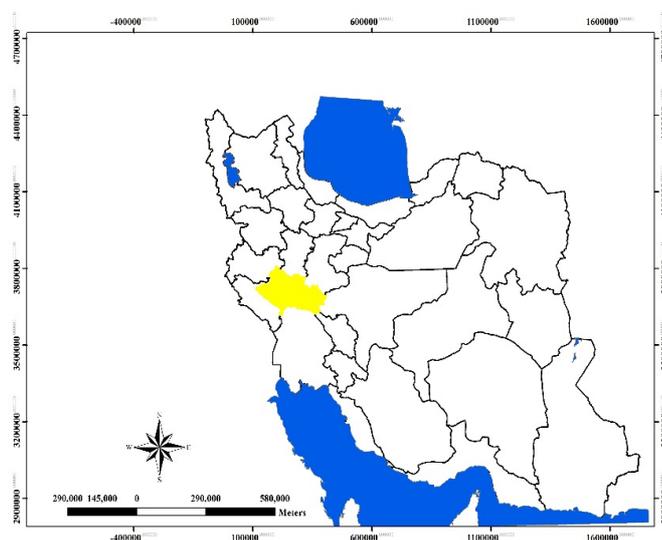
infections is different in different geographical areas [18].

Therefore, regarding the limited number of studies conducted in this field in Iran [19], and also due to the lethal effect of these infections on individuals, high costs of treatment and their destructive social effects, the present study was conducted to determine HBV / HIV and HCV / HIV co-infection. It was also done in order to determine the risk factors of HBV and HCV transmission in Lorestan province.

2. MATERIALS AND METHODS

2.1. Study area

Lorestan province is located in the southwest of Iran, bordering with the states of Markazi, Hamedan, Kermanshah, Khuzestan, Ilam, and Isfahan. The estimated population of Lorestan is 1,754,243. The district covers an area of approximately 28,294 km² [Figure 1]. The province comprises of 11 counties, 29 districts, and 85 habitations. (Source:



http://amar.sci.org.ir/index_e.aspx).

Figure 1- Location of Lorestan province within Iran.

2.2. Study design and patients

The present cross-sectional study conducted on all the patients suffering from HCV and HBV visiting infectious Clinic in Khorramabad city from September 2014 to September of 2016. And at the next stage, they were referred to high-risk

behavior counseling centers in the city. The centers tried to collect demographic and epidemiological information such as age, sex, and to determine possible ways of transmission (history of transfusion of blood and its products, IV drug abuse, risky sexual behaviors, needle stick accidents, venesection and tattooing, and unsafe dental and surgical procedures) for each patient. Then, the patients were referred to the pathobiology labs throughout the city to conduct laboratory supplementary studies.

2.3. Laboratory tests

All the samples were analyzed using ELISA technique to detect HBS Antigen (Pishtaz Teb Diagnostics, Iran), HIV-antibody (Ab) (Wantai, China) and HCV-Ab (Diaplus, Italy). In the present research, the patients whose blood serum was positive regarding Hepatitis B virus surface antigen (HBS-Ag) were recognized as Hepatitis B infection regardless of the duration and stages of disease. In addition, the patients whose blood serum was positive regarding Hepatitis C virus surface antigen were recognized as Hepatitis C infection regardless of the duration and stages of disease. In some cases, Molecular confirmatory tests were done. The cases with positive serum regarding anti-HIV antibodies were considered as HIV infection regardless of the presence or absence of clinical symptoms. Moreover, the confirmatory test was positive for all the cases.

2.4. Statistical analysis

All statistical analyses were performed using SPSS software for Windows. Univariate analysis using chi-square or Fisher's exact tests were done to assess the association between infection status and associated risk factors, and $P < 0.05$ was set as the significant level of differences.

2.5. Ethical consideration

Approval of the study protocol was obtained from the Ethical Review Board of Lorestan University of Medical Sciences. Written informed consent was obtained from all the study participants or their parents/guardians.

3. RESULTS

3.1. Socio-demographic Characteristics of the Study Participants

Out of a total of 373 patients in this study, 252 of them (67.56%) were male and 121 (32.44%) were female. The mean age of the patients was 38.5 ± 12.3 years. The mean age of HBV positive (38.5 ± 13.4 years) and HCV positive (41.2 ± 9.8 years) patients did not have any significant difference (P -Value=0.342).

3.2. Prevalence of HIV, HCV, and HBV Infections

In this research, 80.7% of patients (301 patients) were suffering from HBV, 15% (56 patients) from HCV, and 4.3% (16 patients) from HCV and HBV co-infection. Of 42 patients (11.26 percent) with Cirrhosis, 36 patients (9.65%) of them were HBV positive and 6 patients (1.61%) were HCV positive; But this difference was not statistically significant (P -Value=0.162). Also, of 4 patients (1.07%) with Hepatocellular carcinoma (HCC), 3 of them (0.80%) were HBV positive and 1 patient (0.27%) was HCV positive; This difference was not statistically significant (P -Value=0.631).

3.3. Prevalence of HIV/HCV, HCV/HBV, and HIV/HCV/HBV Co-Infection

In this survey, all the patients were examined regarding HIV infection. In 28 patients (7.51%), testing was not possible at the first stage because of insufficient samples; as a result, they were tested again. The conducted tests indicated that there was not concurrent HIV infection in HBV positive patients. On the other hand, in HCV positive patients, 9 patients (16.07 percent) were concurrently infected with HIV, in addition, of 16 patients with HBV/HCV co-infection, one patient (6.25 percent) was infected by HIV.

3.4. Risk Behaviors Associated with HBV, HCV and HIV

All the patients with HIV infection in this study mentioned the history of IV drug abuse, and three of them mentioned multiple unsafe sexual relationships in addition to the history of IV drug abuse. In terms of risk factors of HBV transmission, it was observed that the most

common risk factors included positive family history (37.85%), history of venesection and tattooing (14.51%), and unsafe surgical procedures (13.25%). Moreover, in those with HCV infection, a history of IV drug abuse (36.11%) was the most common risk factor, followed by a history of blood transfusion (23.61%), and unsafe sexual relationship (22.22%). **Tables 1 and 2** represent detailed information about the frequency of transmission risk factors in patients with HBV and HCV infections.

In the present study, out of 16 patients suffering from HBV/HCV co-infection, 9 people mentioned a history of IV drug addiction, 3 people had a history of tattooing, 2 people had a history of unsafe sexual behaviors, and one person mentioned the history of needle stick accident. One person in this group did not mention any clear risk factor.

Table 1- Frequency distribution of transmission risk factors in the patients with HBV infection (317 persons)

Transmission risk factors	Number (%)
Positive Family history (other than spouse)	120 (37.85)
Suffering wife	15 (4.73)
History of Surgery	42 (13.25)
History of venesection and tattooing	46 (14.51)
History of visiting the dentist	27 (8.52)
History of blood transfusion	25 (7.89)
History of IV drug abuse	9 (2.84)
History of Needles stick accident	5 (1.58)
History of Unsafe sexual relationship	3 (0.95)
Unknown	79 (24.92)

Because there is more than one risk factor in a number of patients, the total is more than 100 percent.

Table 2- Frequency distribution of transmission risk factors in the patients with HCV infection (72 persons)

Transmission risk factors	Number (%)
Positive Family history (other than spouse)	2 (2.78)
Suffering wife	1 (1.39)
History of Surgery	8 (11.11)
History of venesection and tattooing	10 (13.89)
History of visiting the dentist	6 (8.33)
History of blood transfusion	17 (23.61)
History of IV drug abuse	26 (36.11)
History of Needles stick accident	2 (2.78)
History of Unsafe sexual relationship	16 (22.22)
Unknown	1 (1.39)

Because there is more than one risk factor in a number of patients, the total is more than 100 percent.

4. DISCUSSION

The present study was conducted to determine HBV/HIV and HCV/HIV co-infection. It was also done in order to determine the risk factors of transmission of HBV and HCV in Lorestan province. The concurrent infection has a significant role in prognosis of patients, and the rate of progression of hepatic disease toward fibrosis [20]. HCV/HIV co-infection leads to activation of Hepatitis C, followed by acceleration of process toward cirrhosis by increasing profibrogenic cytokines and oxidative stress, as well as acceleration of the outbreak of hepatocellular carcinoma [21]. In addition, the effects related to antiretroviral anti- HIV drugs on liver and the pathologic role of the HIV virus on liver are important [22].

On the other hand, the patients with HBV/HIV co-infection have higher morbidity and mortality that is because of increased viral load of HBV and increased risk of cirrhosis [23]. However, by advent of effective anti-viral drugs like Tenofovir, the mortality has decreased [24].

The findings of this study indicated that HIV prevalence in patients with hepatitis C was about 18.33%; any case of HIV in HBV positive patients was not reported. In addition, among 16 patients suffering from HBV/HCV co-infection, one patient (6.25%) was infected by HIV. While in the study of Afsharian et al in Kermanshah city (west of Iran), 42.62% of patients [25] and in the study of Mokhtarifar et al in Mashhad city (north-east of Iran) 0.9% of patients [26] were suffering from HCV/HIV co-infection. On the other hand, in the study of Tahaei et al in Tehran on 264 patients with HBV, the rate HBV/HIV co-infection was reported as 0.37% and the HBV/HCV co-infection was 4.6%. Also, there was no HBV/HCV/HIV co-infection in this study [19]. In addition, in Babamahmoodi et al's study in Mazandaran province on 186 patients with HIV, it was observed that 11.3% of patients were HBV/HIV positive, and 33.5% HCV/HIV positive [24]. In a survey carried out in Ahvaz city (southwest of Iran), the co-infection rates of HBV,

HCV, and HBV/HCV in HIV patients was respectively 44%, 74% and 20% [27]. In another study on the hemodialysis patients in Kerman (Center of Iran), the rate of HBV infection was about 7 percent, the rate of HCV infection was about 7 percent and the rate of HCV/HBV co-infection was about 1.7 percent, however, any case of HIV was not observed [28]. As IV drug addiction is one of the main methods of HIV and HCV transmission, in a survey on 155 male IV drug users, HBV/HCV/HIV co-infection has been reported as 1.3 percent [29]. In another study by Valizadeh et al in the western Azerbaijan (north-west of Iran) that has been conducted on 35 patients with hemophilia, 8.5 percent of them were HCV positive, and any case of HBV/HIV co-infection was not observed in these patients [30]. In other parts of the world, there are few studies. For example, in a prospective descriptive study conducted for one year in 24 research centers in America, of 3350 people with HCV, 8.4 percent of them were HCV/HIV positive [16]. In some African countries, some studies have been conducted on HIV positive patients; the risk of HBV/HIV co-infection in these studies was about 5.2 to 5.4 percent and the risk of HCV/HIV co-infection was about 3.7 to 5.8 percent [31-33]. Therefore, it is clear that the prevalence of HBV/HIV and HCV/HIV co-infection is different in different geographical areas, the difference that could be due to differences in known risk factors of transmission.

In the present study, the most common risk factors of HBV transmission were positive family history (37.85%), history of venesection and tattooing (14.51%), and history of surgery (13.25%), that these findings were similar to other studies in different provinces of Iran [26, 34].

Therefore, it must be considered that although the unsafe sexual relationship is one of the most important methods of infection transmission in western countries, the percentage is negligible in Iran (0.95% in this study) [1, 2]. In addition, as venesection and tattooing are the second risk factors of HBV transmission in this region, a full

supervision must be taken over the centers that do these actions.

In present study, the most common risk factors of HCV transmission included IV drug abuse (36.11%), history of blood transfusion (23.61%) and unsafe sexual relationship (22.22%). In other similar studies in Iran, IV drug abuse reported as the most common risk factor of HCV transmission [35, 36].

Finally, it is important to mention that due to ethical issues and social limitations in Iran, the patients infected by hepatitis and HIV might have avoided telling correct information especially about high risk sexual behaviors. Moreover, a number of patients with HIV avoided taking part in the study due to wrong social attitude toward them and social problems. The mentioned reasons can distort the information and results of this study.

5. Conclusion

Taking into consideration the risk factors for HBV and HCV infections, education about their transmission routes and prevention are emphasized.

Conflict of interest

The authors declare no conflict of interests.

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REFERENCES

1. Lavanchy D, Kane M. Global Epidemiology of Hepatitis B Virus Infection. In: Liaw Y-F, Zoulim F, editors. Hepatitis B Virus in Human Diseases. Cham: Springer International Publishing; 2016. p. 187-203.

2. Salehi-Vaziri M, Sadeghi F, Almasi Hashiani A, Gholami Fesharaki M, Alavian SM. Hepatitis B Virus Infection in the General Population of Iran: An Updated Systematic Review and Meta-Analysis. *Hepat Mon.* 2016 April; 16 (4): e35577.
3. Bostan N, Mahmood T. An overview about hepatitis C: a devastating virus. *Crit Rev Microbiol.* 2010; 36(2):91–133.
4. Khaja MN, Madhavi C, Thippavazzula R, Nafeesa F, Habib AM, Habibullah CM, et al. High prevalence of hepatitis C virus infection and genotype distribution among general population, blood donors and risk groups. *Infect Genet Evol.* 2006; 6 (3): 198-204.
5. Alavian SM, Adibi P, Zali MR. Hepatitis C virus in IRAN: Epidemiology of an emerging infection. *Arch Iranian Med.* 2005; 8 (2): 84-90.
6. Keyvani H, Alizadeh H, Alavian SM. Distribution frequency of hepatitis C virus genotype in 2231 patients Iran. *Hepato Res.* 2007; 37: 101-3.
7. Svrtlih N, Delic D, Simonovic J, Jevtovic D, Dokic L, Gvozdenovic E, et al. Hepatitis C virus genotypes in Serbia and Montenegro: The prevalence and clinical significance. *World J Gastroenterol.* 2007; 13 (3): 355-60.
8. Nazer MR, Beiranvand B, Obeidavi Z, Beiki O. Prevalence of hepatitis C genotypes in patients with hepatitis C in Lorestan province (2009-2013). *J Kermanshah Univ Med Sci.* 2014; 18(2): 108-113.
9. Vossughinia H, Goshayeshi LA, Rafatpanah Bayegi H, Sima H, Kazemi A, Erfani S, et al. Prevalence of Hepatitis C Virus Genotypes in Mashhad, Northeast Iran. *Iran J Public Health* 2012; 41: 56-61.
10. Samimi-Rad K, Nategh R, Malekzadeh R. Molecular epidemiology of hepatitis C virus in Iran as reflected by phylogenetic analysis of the NS5B region. *J Med Virol.* 2004; 74: 246-52.
11. Fauci AS, Folkers GK. Toward an AIDS-free generation. *Jama* 2012; 308: 343-4.
12. Highleyman L. HIV and Hepatitis C Co-infection. *BETA* 2003; 15: 32-44.
13. Park JS, Saraf N, Dielerich DT. HBV plus HCV, HCV plus HIV, HBV plus HIV. *Curr Gastroenterol* 2006; 8: 67-74.
14. Sheng WH, Chen MY, Hsieh SM, Hsiao CF, Wang JT, Hung CC, et al. Impact of chronic hepatitis B virus (HBV infection) on outcomes of patients infected with HIV in an area where HBV infection is hyperendemic. *Clin Infect Dis* 2004; 38: 1471-7.
15. Karura JW, Lule GN, Joshi M, Anzala O. Prevalence of HCV and HCV/HIV co-infection among volunteer blood donors and VCT Clients. *East Afr Med J* 2005; 82: 166-90.
16. Bini EJ, Currie SL, Shen H, Bran N, Schmidt W, Anand BS, et al. National multicenter study of HIV testing and HIV seropositivity in patients with chronic hepatitis C virus infection. *J Clin Gastroenterol* 2006; 40: 732-9.
17. Kim JH, Psevdos G Jr, Sharp V. Five-Year Review of HIV Hepatitis B Virus (HBV) Co-Infected Patients in a New York City AIDS Center. *J Korean Med Sci* 2012; 27: 830-3.
18. Rouet F, Chaix ML, Inwoley A, Msellati P, Viho I, Combe P, et al. HBV and HCV prevalence and viremia in HIV positive and HIV-negative pregnant women in Abidjan, Cote d Ivoire: the ANRS 1236 study. *J Med virol* 2004; 74: 34-40.
19. Tahaei SM, Mohebbi SR, Azimzadeh P, Vahedi M, Almasi S, Romani S, et al. Frequency of HIV and HCV Co-Infections in Chronic HBV Patients Referred to Taleghani Hospital, Tehran, Iran from 2006 to 2010. *Hepat Mon* 2011; 11: 993-6.
20. Lavanchy D. Hepatitis B virus epidemiology, disease burden, treatment, and current and emerging prevention and control measures. *J Viral Hepat* 2004; 11: 97-107.
21. Lin W, Weinberg EM, Chung RT Pathogenesis of accelerated fibrosis in HIV/HCV co-infection. *J Infect Dis* 2013; 207 Suppl 1: S13-8.

22. Curry MP. HIV and hepatitis C virus: special concerns for patients with cirrhosis. *J Infect Dis* 2013; 207 Suppl 1: S40-4.
23. Thio CL, Seaberg EC, Skolasky R Jr, Phair J, Visscher B, Muñoz A, et al. HIV-1, hepatitis B virus, and risk of liver related mortality in the Multicenter Cohort Study (MACS). *Lancet* 2002; 360: 1921-6.
24. Babamahmoodi F, Heidari Gorji MA, Mahdi Nasehi M, Delavarian L. The prevalence rate of hepatitis B and hepatitis C co-infection in HIV positive patients in Mazandaran province, Iran. *Med Glas (Zenica)* 2012; 9: 299-303.
25. Afsharian M, Raoufi R, Vaziri S, Janbakhsh AR, Mansouri F, Ghadiri K, Saiad B, Leghaei Z. HCV genotypes in patients referred to Sina hospital in Kermanshah during 2005 to 2006. *Journal of infectious and tropical disease*. 2007; 39: 19-23.
26. Mokhtarifar A, Rezvani HR, Esmailzadeh A, Ghaffarzadegan K, Goshayeshi L. The Prevalence of HIV and Transmission Risk Factors among Hepatitis B and C Patients Referred to Emam Reza Hospital, Mashhad, Iran from 2005-2008. *Govaresh* 2014; 19: 14-9. [In Persian]
27. Alavi SM, Etemadi A. HIV/HBV, HIV/HCV AND HIV/HTLV-1 co-Infection among Injection Drug User Patients Hospitalized at the Infectious disease ward of training Hospital in Iran. *Pak J Med Sci* 2007; 23: 510-3.
28. Zahedi MJ, Darvish Moghaddam S, Alavian SM, Dalili M. Seroprevalence of Hepatitis Viruses B, C, D and HIV Infection Among Hemodialysis Patients in Kerman Province, South-East Iran. *Hepat Mon* 2012; 12: 339-43.
29. Sofian M, Aghakhani A, Banifazl M, Azadmanesh K, Farazi AA, McFarland W, et al. Viral hepatitis and HIV infection among injection drug users in a central Iranian City. *J Addict Med* 2012; 6: 292-6.
30. Valizadeh N, Nateghi S, Noroozi M, Hejazi S, Aghanezhad F, Ali AA. Seroprevalence of hepatitis C, hepatitis B and HIV viruses in hemophiliacs born 1985-2010 in west Azarbaijan of Iran. *Asian J Transfus Sci* 2013; 7: 55-8.
31. Rebbani K, Ouladlhasen A, Bensghir A, Akil A, Lamdini H, Issouf H, et al. Co-infections with hepatitis B and C viruses in human immunodeficiency virus-infected patients in Morocco. *Clin Microbiol Infect* 2013; 19: E454-7.
32. Rusine J, Ondoa P, Asiimwe-Kateera B, Boer KR, Uwimana JM, Mukabayire O, et al. High Seroprevalence of HBV and HCV Infection in HIV-Infected Adults in Kigali, Rwanda. *PLoS One* 2013; 8: e63303.
33. Karuru JW, Lule GN, Joshi M, Anzala O. Prevalence of HCV and HCV/HIV co-infection among in-patients at the Kenyatta National Hospital. *East Afr Med J* 2005; 82: 170-20.
34. Alavian SM, Tabatabaei SV, Ghadimi T, Beedrapour F, Kafi- Abad SA, Gharehbaghian A, et al. Seroprevalence of Hepatitis B Virus Infection and Its Risk Factors in the West of Iran: A Population-based Study. *Int J Prev Med* 2012; 3: 770-5.
35. Hajjani E, Hashemi J, Masjedizadeh R, Shayesteh AA, Idani E, Rajabi T. Seroepidemiology of hepatitis C and its risk factors in Khuzestan Province, south-west of Iran: a case-control study. *World J Gastroenterol*. 2006; 12 (30): 4884-7.
36. Alavian SM, Gholami B, Masarrat S. Hepatitis C risk factors in Iranian volunteer blood donors: a case-control study. *J Gastroenterol Hepatol* 2002; 17: 1092-7.