Shiraz E-Med J. 2015 April; 16(4): e24676. DOI: 10.17795/semj24676

Published online 2015 April 23. **Research Article**

Hepatitis B Virus Infection Serology and the Associated Risk Factors Among Patients With HIV in Shiraz, Iran

Mohammad Ali Davarpanah [1]; Nasrin Motazedian [1,*]; Ebrahim Fallahzadeh [2]; Maryam Rasti [2]; Hashem Rahmati [3]; Nadia Motazedian [1]

[1]Shiraz HIV/AIDS Research Center, Shiraz University of Medical Sciences, Shiraz, IR Iran
[2]Gastroenterohepatology Research Center, Shiraz University of Medical Sciences, Shiraz, IR Iran
[3]Faculty of Nursing and Midwifery, Shiraz University of Medical Sciences, Shiraz, IR Iran

*Corresponding Author: Nasrin Motazedian, Shiraz HIV/AIDS Research Center, Shiraz University of Medical Sciences, Shiraz, IR Iran. Tel/Fax: +987137386272, E-mail: motazediann@yahoo.com

Received: October 18, 2014; **Revised:** January 3, 2015; **Accepted:** January 9, 2015

Background: Human Immunodeficiency Virus-1 (HIV-1) and Hepatitis B Virus (HBV) are transmitted through common routes; therefore, simultaneous infection with both viruses is common.
Objectives: The current study aimed to determine HBV infection serological profile and the associated risk factors among HIV positive individuals in Shiraz.
Patients and Methods: In this cross-sectional study, 186 HIV infected individuals above 18 years old, referring to Shiraz Voluntary Counseling and Testing Center from 2010 to 2011were enrolled. All participants were assessed for the serological status of HBV infection using Hepatitis B surface antigen, Hepatitis B surface antibody, Hepatitis B core antibody levels, and HBV Polymerase Chain Reaction.
Results: A total of 186 HIV positive individuals eligible for analysis including 164 (88.2%) males and 22 (11.8%) females were selected for the study. Hepatitis B surface antigen (HBsAg), Hepatitis B surface antibody (HBsAb) and Hepatitis B core antibody (HBcAb) were detected in 66 (35.5%), 62 (41.3%), and 39 (21%) subjects, respectively. HBV DNA was detected in 39 subjects (21%).
Conclusions: The current study showed that less than half of the HIV positive participants had evidence of previous exposure to HBV. Also, the risk of chronic HBV was higher in the subjects than the normal population. It is suggested to educate HIV positive individuals regarding prevention and transmission of other viral infections such as HBV, HCV, and compliance with their medication.

Keywords: Co-infections; HIV; Risk Factors

1. Background

Human Immunodeficiency Virus-1 (HIV-1) and Hepatitis B Virus (HBV) are transmitted through a common route; therefore, simultaneous infection with both viruses is common. Approximately, 10% of the 40 million HIV positive individuals in the world have chronic Hepatitis B infection. Death from Acquired Immune Deficiency Syndrome (AIDS)-related illnesses has declined since the introduction of Highly Active Antiretroviral Therapy (HARRT) in the industrialized countries. Liver disease has replaced the classical opportunistic complications of severe immunodeficiency state. In contrast to mono-infection with HIV, Hepatitis B, and HIV, co-infection has higher liver related mortality rate even in the presence of antiviral drug use. There are several reasons to highlight the role of HIV infection in the natural history of hepatitis; they include the increased number of persistent infection, higher HBV DNA level, lower rate of HBe antigen clearance, progression to liver cirrhosis, liver-related mortality, and increased risk of hepatocellular carcinoma at lower CD4 T cell count (1, 2). The prevalence of chronic hepatitis depends on age at the time of infection and the mode of HBV transmission, which varies from region to region. Different regions of the world reported various prevalence of chronic HBV infection from high (> 8%), intermediate (2 - 7%), to low (< 2%). Prenatal transmission is the main route of HBV transmission in areas with high HBV endemicity; whereas in low endemic areas, HBV infection occurs in well-defined high-risk groups such as, intravenous drug users (IDUs), male having sex with males (MSM), health care workers, and regular recipients of blood or patients going under hemodialysis (3). According to a HIV cohort study in the US, among 2769 participants, 1078 (38.9%) had HBV infection in the observation course. Chronic Hepatitis B was detected in 117 (10.9%) patients with HIV under the study. Therefore 40% of the co-infection with both viruses was detected each year. However, a similar study also from the US showed HIV/HBV co-infection in 4.47% of HIV positive individuals. HIV/HBV co-infections were associated with males, black race, MSM, (Intravenous Drug User) IDU, concurrent IDU, and heterosexual activity or unknown in New York City (4, 5). Studies from Nigeria, Botswana, and Brazil showed

the prevalence of Hepatitis B surface antigen (HBsAg) 6.6%, 5.3%, and 4.7%, respectively. The result of risk factor analysis showed that infection through male homosexual contact had the highest rate, 64 (74.4%), and 16 (18. 6%) were IDUs (6-8). Serological studies of exposure to HBV from the South and North of Iran respectively showed a prevalence of 44.23%, and 9.4% HBsAg among HIV positive individuals. Out of 150 HIV-positive individuals, 55% were IDUs, and 74% of the 86 patients had a history of incarceration (9, 10). Isolation of anti-HBc indicated the presence of Hepatitis B core antibody (anti-HBc) in the absence of HBsAg and anti-HBs. It was the second most common serological pattern of HBV infection found in 30% of the patients with HBV (11). Diagnosis of HBV infection is based on the presence of HBsAg and anti-HBc. Anti-HBc is found in the acute phase of infection and is sustained for a long time after clearance of virus from the patient's body. Presentation of HBsAg and anti-HBc (IgM) at the same time shows current infection. If anti-HB is present with anti-HBc, it demonstrates a past removed infection (12). A survey on 170 HIV positive individuals found that anti- HBc was positive in 115 (68%) subjects. Meanwhile, HBsAg, anti-HBs and anti-HBc alone were detected in 12%, 52%, and 35% of the participants, respectively (12). Moreover, a study in Tehran, Iran, showed a 20.75% prevalence of anti-HBc among HIV positive individuals, and 13.6% of them were DNA positive HBc (13). Researchers in India reported the 7.28% prevalence of HBsAg in patients with HIV, which was seven times more than that of the HIV negative control group. This study showed the prevalence of 24.5% and 20.7% occult HBV infection (HBV- DNA positive) in anti-HBc and anti HBs positive individuals, respectively (14). Iran is classified as low endemic area for Hepatitis B infection. Interestingly, epidemiological changes indicate that the average age of infection is increasing and the transmission route is changing from vertical to horizontal (15). Patients with HIV have higher serological prevalence of anti-HBc and HBsAg than the groups of non-HIV-infected individuals in the same geographic area, due to common routes of HBV and HIV transmission (12). Numerous consensus studies have focused on the importance of co-infection, the effect of HIV infection on HBV, and also the importance of checking anti HBc level before HBV vaccination. Evaluation of HBV risk factors is an important point to control the disease.

2. Objectives

The current study aimed to determine HBV infection serological profile and determine the associated risk factors among HIV positive individuals in Shiraz, Iran.

3. Patients and Methods

The current cross-sectional study among HIV positive individuals referring to Shiraz Voluntary Counseling and Testing (VCT) Center in one year from 2010 to 2011; 186 individuals with HIV over 18 years old were selected through random sampling. HIV infection was confirmed by ELISA (BIORED, France) and western blot tests (GENELABS, Singapore) in all individuals who referred to the VCT. The HIV positive individuals who did not wish to participate in the study were replaced by the next person. The study was approved by the Medical Ethics Committee of Shiraz University of Medical Sciences. After obtaining an informed consent form from each individual, data was collected using data collecting form. The studied variables included gender, age, information about history of imprisonment, prenatal transmission, injection of drugs, blood and blood product transfusion, high risk partner, partner with HIV, tattooing in prison and out of prison, sharing razor in prison and out of prison, evidences of sexual transmitted infection, surgery, and stab wound. All participants were assessed for the serological status of HBV infection using HBsAg, HBsAb and HBcAb level. HBV Polymerase Chain Reaction (PCR; HBV qualitative, Cinnagen. Iran, Tehran) was performed to determine the current active HBV infection. Blood samples were tested for HBsAg, by ELISA (BEHRING, Germany), and then HBsAg sero-negative patients were tested for HBsAb and HBcAb with the same technique in Shiraz Gastro-enterohepatology Research Center. Statistical analysis was performed using SPSS software, version 15. Descriptive and logistic regression tests were performed for analysis. A P value of < 0.05 was considered as significant.

4. Results

A total of 186 HIV positive individuals eligible for analysis including 164 (88.2%) males and 22 (11.8%) females entered the study. The mean age of the participants was 37 ± 7.95 years with a range of 18 to 68 years. The most common routes of HIV transmission among all volunteers were drug injection and having sex with HIV positive partners, which were observed in 136 (73.1%) and 20 (10.8%) of the participants, respectively. HBsAg, HBsAb and HBcAb were detected in 66 (35.5%), 62 (41.3%), and 39 (21%) of participants, respectively. Among individuals with HBs antigenemia 64 (97%), and 2 (3%) were males and females, respectively. HBsAb was detected in 55 (88.7%) males and 7 (11.3%) females. Drug injection was the most common risk factor among the HBsAg positive individuals, observed in 52 patients (78.8%). Anti-HBc was detected in 38 (97.4) males and one (2.6) female; IDU was the most common route of transmission in 29 (74.4%). HBV DNA was detected in 39 subjects (21%) who were also positive for HBsAg and HBcAb. Among the participants with positive HBV DNA, 13 (41.9%) were HBsAb positive. Out of the 39 HBcAb positive subjects, 13 (41.9%) were positive for HBsAb. Among the HBsAg positive subjects, 39 (59.1%) were positive for HBc Ab. Among the subjects with positive HBsAg, 19 (36.5%) were positive for HBsAb. Prevalence of the associated risk factors among the participants is listed in Table 1. Logistic regression was done to find the relationship between risk factors (age, gender, history of imprisonment, perinatal transmission, injection of drugs, blood and blood product transfusion,

Table 1. HIV-HBV Co-infection Based on the Risk Behaviors Associated With HIV Infection [a]

History of High Risk behaviors	HIV^+	HIV/ $HBVco^-$ Infection $HBsAg^+$
Incarceration	151 (81.2)	57 (86.4)
Drug injection	137 (73.7)	53 (80.3)
Heterosexual contact	76 (40.9)	29 (43.9)
Blood transfusion	29 (15.6)	9 (13.6)
HIV^+ partner	22 (11.8)	3 (4.5)
Evidences of sexual transmitted infection	12 (6.5)	4 (6.1)
Tattooing (in prison)	51 (27.4)	15 (22.7)
Tattooing (out of prison)	62 (33.3)	27 (40.9)
Sharing razor (in prison)	75 (40.3)	34 (51.5)
Sharing razor (out of prison)	12 (6.5)	9 (13.6)
Stab wound	5 (2.7)	3 (4.5)
Surgery	14 (7.5)	5 (7.6)
Homosexual contact	4 (2.2)	2 (3)

[a] Data are presented as No. (%)

high risk partner, partner with HIV, tattooing in prison and out of prison, sharing razor in prison and out of prison, evidences of sexual transmitted infection, surgery, and stab wound) and serological markers (HBsAg and HBcAb). There was a relationship between sharing razor out of prison, and HBs Ag (OR 4.45; %95 CI 1.02-19.36, P = 0.04). No significant relationship was found between HBcAb and the risk factors.

5. Discussion

There are various scenarios for HIV/HBV acquisition in different parts of the world. In the current study, IDU was the most common route of transmission but sharing razors had positive effect on HIV/HBV transmission. Studies from different parts of Iran showed that IDUs had the highest prevalence among HBV/HIV co-infected individuals similar to the current study (16-18). The main route of blood born viral infection transmission in Iran is IDUs; therefore, screening for HCV, HBV and HIV in high risk populations and development of VCT centers and STD clinic for the high risk groups are suggested (18, 19). The current study showed a lower prevalence of HBsAg in Shiraz than the other parts of Iran (9, 16). The prevalence of HBsAg was higher than those of different regions of the world and also Iran (4, 6, 10, 14, 20-22). In sub-Saharan Africa where both HIV and HBV are endemic, the HBsAg prevalence among individuals with HIV was less than our study (23). A study from Taiwan showed opposite observations in HBsAg and anti-HBc frequency than those of the current study (24). A study on the prevalence and correlated factors of chronic Hepatitis B infection among the Brazilian patients with HIV showed that chronic HBV was associated with intravenous drug use, male gender, STI associated with HIV diagnosis, and death. Illicit drug use in the current study was higher than the Brazilian patients, but the other risk factors such as having sex with male, and the history of STI was higher than those of the current study (25). In the United States, MSMs and IDUs have the highest prevalence in HIV/HBV co-infection. In contrast, in Asia and Sub-Saharan Africa overall prevalence of HBV is higher than other parts of the world where vertical transmission and early childhood exposure are the most common transmission modes, respectively; HBV prevalence among patients with HIV is even higher about 20% - 30% (3). Interestingly, a study from China concluded that sociodemographic characteristics and mode of HIV transmission were not significantly correlated with co-infections of HBV/HIV, and the route of HIV transmission varied widely in the four provinces under the study (20). In Afghanistan, no sociodemographic variables were significantly associated with HIV or HBsAg positivity, but sharing needles and injecting drugs in prison were the main causes (21). Another serologic marker that becomes positive in HBV infection and persists for a long time is HBc antibody. A study conducted in Iran showed that the prevalence of HBc antibody alone and HBV-DNA were higher than those of the current study (13). The current study did not detect isolated HBcAb in any of the subjects. All 39 subjects with positive HBcAb showed HBsAg (Table 2). Subjects with immune deficiency induced by HIV may present atypical results in serological tests for Hepatitis B Virus (1). Patients with HBV who were immune deficient often showed mild acute liver injury but were major chronic carriers (26). Concurrently positive HBsAg and HBsAb were found among 19 (11%) individuals that may be due to dual infection with different HBV serotypes. Finally, using PCR method HBV-DNA was detected in 39 (59.1%) HBsAg and 13 (21%) HBsAb positive subjects. Results of the current study showed higher concurrent HBsAg and anti-HBs than other studies. The mechanism underlying the presence of both HBsAg and anti-HBs antibodies remains unknown, but immune-escape HBV

Table 2. Status of Individuals With HIV Based on Laboratory Data

Tests Results	No. (%)	Interpretation
HBsAg (+) **and PCR** (+)	39 (21)	Viremic patients
HBsAg (+) **and PCR** (-)	27 (14.5)	Non-viremic patients
HBsAg (-) **and HBsAb** (-) **andHBcAb** (+)	0 (0)	Anti-HBc alone patient
HBsAg (-) **andHBsAb** (+) **andHBcAb** (-)	39 (23.6)	Immune, might be due to vaccination
HBsAg (+) **and HBsAb** (+)	19 (36.5)	might be immune-escape Hepatitis B virus mutants

mutants might be an explanation (27, 28). Another serologic marker that becomes positive in HBV infection and persists for long time is HBc antibody. A major challenge in management of hepatitis B is the Occult HBV Infection (OBI), which is simply defined as serologically undetectable Hepatitis B surface antigen (HBsAg-ve) despite the presence of circulating HBV DNA. Most of the OBI carriers have very low level of viremia. Therefore, detection of this infection needs sensitive HBV-DNA PCR assay. OBI is common among patients with HIV. Therefore it is very important to screen the these individuals for resolved or active HBV infection, diagnosis, and treatment of OBI (29). According to this definition, the current study did not find OBI in the participants of the study. No HBcAb was detected in any of the subjects. All 39 subjects with positive HBcAb showed HBsAg. In Sub-Saharan Africa, HBV DNA detection was higher than the current study (23). A study in Iran showed higher prevalence of HBc antibody alone and HBV-DNA, compared to the current study (13). The Swiss cohort study showed anti-HBcAg persisted as single marker of HBV infection in majority of the patients during three years of follow up (30). The current study showed that 43 (26.2%) of the participants with HIV had evidence of previous exposure to HBV (HBsAg negative and HBsAb positive). Risk of chronic HBV in the current survey was higher than that of the normal population (31). HIV/HBV co-infection is a major health problem. Patients with HIV/HBV co-infection experience rapid disease progression and higher frequency of liver complications such as cirrhosis and hepatocellular carcinoma (32). Laboratory and clinical management of HBV/HIV co-infection should contain HBeAg, anti-HBe and HBVDNA, HBV vaccination, blood pictures, clotting profiles including prothrombin time, international normalized ratio (INR), alpha-feto-protein (AFP), liver and renal functions test, and a baseline liver ultrasonography (26). In conclusion, HIV and HBV co-infection is frequently observed due to common route of transmission; new cases of acute HBV infection in known HIV positive patients highlight the importance of educating HIV positive individuals regarding the prevention of transmission. Proper attention to vaccination against HBV in high risk individuals and attempts to treat HBV infection in the setting of HIV infection should be considered. It is recommended to prepare a clinical guideline focusing on HIV/HBV co-infection including screening and management of co-infection. Chronic HBV in HBcAb positive people with HIV should be considered; and more diagnostic evaluations such as HBV PCR and liver ultrasonography should be performed during their clinical management. The individuals with HIV/HBV co-infection must receive antiretroviral regimen, which includes drugs such as tenofovir that affect HBV replication. In the current cross-sectional study, it was difficult to find temporal relationship between HIV infection and HBV. A cohort study should be conducted to determine the reliability and validity of the patterns observed in the current study.

Acknowledgements

Authors wish to thank the participants in the study.

Authors' Contributions

Mohammad Ali Davarpanah: study design; Nasrin Motazedian: data analysis, manuscript writing and revising; Ebrahim Fallahzadeh: data collection; Maryam Rasti: data collection; Hashem Rahmati: data collection; Nadia Motazedian: manuscript writing and revising. All authors read and approved the final copy of the manuscript.

References

1. Thio CL. Hepatitis B and human immunodeficiency virus coinfection. *Hepatology.* 2009;**49**(5 Suppl):S138–45.
2. Chen JJ, Yu CB, Du WB, Li LJ. Prevalence of hepatitis B and C in HIV-infected patients: a meta-analysis. *Hepatobiliary Pancreat Dis Int.* 2011;**10**(2):122–7.
3. Hou J, Liu Z, Gu F. Epidemiology and Prevention of Hepatitis B Virus Infection. *Int J Med Sci.* 2005;**2**(1):50–7.
4. Chun HM, Fieberg AM, Hullsiek KH, Lifson AR, Crum-Cianflone NF, Weintrob AC, et al. Epidemiology of Hepatitis B virus infection in a US cohort of HIV-infected individuals during the past 20 years. *Clin Infect Dis.* 2010;**50**(3):426–36.
5. Kim JH, Psevdos G, Suh J, Sharp VL. Co-infection of hepatitis B and hepatitis C virus in human immunodeficiency virus-infected patients in New York City, United States. *World J Gastroenterol.* 2008;**14**(43):6689–93.
6. Adekunle AE, Oladimeji AA, Temi AP, Adeseye AI, Akinyeye OA, Taiwo RH. Baseline CD4+ T lymphocyte cell counts, hepatitis B and C viruses seropositivity in adults with Human Immunodeficiency Virus infection at a tertiary hospital in Nigeria. *Pan Afr Med J.* 2011;**9**:6.
7. Patel P, Davis S, Tolle M, Mabikwa V, Anabwani G. Prevalence of hepatitis B and hepatitis C coinfections in an adult HIV centre population in Gaborone, Botswana. *Am J Trop Med Hyg.* 2011;**85**(2):390–4.
8. Mendes-Correa MC, Pinho JR, Gomes-Gouvea MS, da Silva AC, Guastini CF, Martins LG, et al. Predictors of HBeAg status and hepatitis B viraemia in HIV-infected patients with chronic hepatitis B in the HAART era in Brazil. *BMC Infect Dis.* 2011;**11**:247.
9. Alavi SM, Etemadi A. HIV/HBV, HIV/HCV and HIV/HTLV-1 co infec-

tion among injecting drug user patients hospitalized at the infectious disease ward of a training hospital in Iran. *Pak J Med Sci.* 2007;**23**(4):510–3.
10. Ramezani A, Mohraz M, Gachkar L. Epidemiologic situation of human immunodeficiency virus (HIV/AIDS patients) in a private clinic in Tehran, Iran. *Arch Iran Med.* 2006;**9**(4):315–8.
11. Perez-Rodriguez MT, Sopena B, Crespo M, Rivera A, Gonzalez del Blanco T, Ocampo A, et al. Clinical significance of "anti-HBc alone" in human immunodeficiency virus-positive patients. *World J Gastroenterol.* 2009;**15**(10):1237–41.
12. Santos EA, Yoshida CF, Rolla VC, Mendes JM, Vieira IF, Arabe J, et al. Frequent occult hepatitis B virus infection in patients infected with human immunodeficiency virus type 1. *Eur J Clin Microbiol Infect Dis.* 2003;**22**(2):92–8.
13. Ramezani A, Banifazl M, Eslamifar A, Aghakhani A. Serological pattern of anti-HBc alone infers occult hepatitis B virus infection in high-risk individuals in Iran. *J Infect Dev Ctries.* 2010;**4**(10):658–61.
14. Gupta S, Singh S. Occult hepatitis B virus infection in ART-naive HIV-infected patients seen at a tertiary care centre in north India. *BMC Infect Dis.* 2010;**10**:53.
15. Alavian SM, Fallahian F, Lankarani KB. The changing epidemiology of viral hepatitis B in Iran. *J Gastrointestin Liver Dis.* 2007;**16**(4):403–6.
16. Mohammadi M, Talei G, Sheikhian A, Ebrahimzade F, Pournia Y, Ghasemi E, et al. Survey of both hepatitis B virus (HBsAg) and hepatitis C virus (HCV-Ab) coinfection among HIV positive patients. *Virol J.* 2009;**6**:202.
17. Mohammad Nejad E, Ehsani SR, Rabirad N, Deljo R, Ranjbarn S, Rezaee S, et al. Prevalence of HBV in HIV Patients Referred to Imam Khomeini Hospital, Tehran, Iran from 2008-2010. *Iran Red Crescent Med J.* 2013;**15**(4):379–80.
18. Keramat F, Eini P, Majzoobi MM. Seroprevalence of HIV, HBV and HCV in Persons Referred to Hamadan Behavioral Counseling Center, West of Iran. *Iran Red Crescent Med J.* 2011;**13**(1):42–6.
19. Vaziri S, Mansouri F, Sayad B, Afsharian M, Janbakhsh A, Karami M. Hepatitis D virus infection among HIV-HBV co-infected patients in Kermanshah, West of Iran. *Hepat Mon.* 2008;**8**(4):252–7.
20. He N, Chen L, Lin HJ, Zhang M, Wei J, Yang JH, et al. Multiple viral coinfections among HIV/AIDS patients in China. *Biosci Trends.* 2011;**5**(1):1–9.
21. Todd CS, Abed AM, Strathdee SA, Scott PT, Botros BA, Safi N, et al. HIV, hepatitis C, and hepatitis B infections and associated risk behavior in injection drug users, Kabul, Afghanistan. *Emerg Infect Dis.* 2007;**13**(9):1327–31.
22. Adoga MP, Banwat EB, Forbi JC, Nimzing L, Pam CR, Gyar SD, et al. Human immunonodeficiency virus, hepatitis B virus and hepatitis C virus: sero-prevalence, co-infection and risk factors among prison inmates in Nasarawa State, Nigeria. *J Infect Dev Ctries.* 2009;**3**(7):539–47.
23. Jobarteh M, Malfroy M, Peterson I, Jeng A, Sarge-Njie R, Alabi A, et al. Seroprevalence of hepatitis B and C virus in HIV-1 and HIV-2 infected Gambians. *Virol J.* 2010;**7**:230.
24. Sheng WH, Kao JH, Chen PJ, Huang LM, Chang SY, Sun HY, et al. Evolution of hepatitis B serological markers in HIV-infected patients receiving highly active antiretroviral therapy. *Clin Infect Dis.* 2007;**45**(9):1221–9.
25. Zago AM, Machado TF, Cazarim FL, Miranda AE. Prevalence and risk factors for chronic hepatitis B in HIV patients attended at a sexually-transmitted disease clinic in Vitoria, Brazil. *Braz J Infect Dis.* 2007;**11**(5):475–8.
26. Ranjbar R, Davari A, Izadi M, Jonaidi N, Alavian SM. HIV/HBV Co-Infections: Epidemiology, Natural History, and Treatment: A Review Article. *Iran Red Crescent Med J.* 2011;**13**(12):855–62.
27. Lada O, Benhamou Y, Poynard T, Thibault V. Coexistence of hepatitis B surface antigen (HBs Ag) and anti-HBs antibodies in chronic hepatitis B virus carriers: influence of "a" determinant variants. *J Virol.* 2006;**80**(6):2968–75.
28. Liu W, Hu T, Wang X, Chen Y, Huang M, Yuan C, et al. Coexistence of hepatitis B surface antigen and anti-HBs in Chinese chronic hepatitis B virus patients relating to genotype C and mutations in the S and P gene reverse transcriptase region. *Arch Virol.* 2012;**157**(4):627–34.
29. Ramezani A, Banifazl M, Mohraz M, Rasoolinejad M, Aghakhani A. Occult hepatitis B virus infection: A major concern in HIV-infected patients: Occult HBV in HIV. *Hepat Mon.* 2011;**11**(1):7–10.
30. Hofer M, Joller-Jemelka HI, Grob PJ, Luthy R, Opravil M. Frequent chronic hepatitis B virus infection in HIV-infected patients positive for antibody to hepatitis B core antigen only. Swiss HIV Cohort Study. *Eur J Clin Microbiol Infect Dis.* 1998;**17**(1):6–13.
31. Alavian SM. Ministry of Health in Iran is serious about controlling hepatitis B. *Hepat Mon.* 2007;**7**(1):3–5.
32. Tahaei SME, 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**(12):993–6.