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Prevalence of hepatitis B (HBV) and C (HCV) viruses co-infections among HIV infected people in Iran

**SeyedAhmad SeyedAlinaghi¹, Pegah Valiollahi¹, Koosha Paydary^{1,2},
Sahra Emamzadeh-Fard^{1,2*} and Minoo Mohraz¹**

¹Iranian Research Center for HIV/AIDS (IRCHA), Tehran University of Medical Sciences, Tehran, Iran.

²Students Scientific Research Center (SSRC), Tehran University of Medical Sciences, Tehran, Iran.

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Infections of human immunodeficiency virus (HIV), hepatitis B (HBV) and C (HCV) viruses are among the grave health concerns confronting global public health. These infections spread via similar routes (e.g. parenteral, sexual and vertical), leading to the anticipation of high prevalence rates of HBV and HCV co-infections among HIV infected patients. HBV and HCV co-infections in HIV-positive patients lead to severe liver disease by means of rapid progression to hepatocellular carcinoma and severe chronic hepatitis. Consequently, the co-infection of these viruses is strongly associated with reduced survival of HIV patients. Various studies have been conducted among Iranian HIV-positive patients to identify HBV/HIV, HCV/HIV and HBV/HCV/HIV co-infection prevalence rates and their correlations. These surveys have been conducted in many cities and a variety of settings throughout the country. These studies have shown that the alarming high rates of HBV/HCV co-infection among HIV patients highlight the need for a timely and systematic assessment of these patients. It is evident that early diagnosis and early start of appropriate treatments could increase the length of life for co-infected HIV patients; therefore, comprehensive identification of risk factors and underlying conditions, as well as HIV treatment, are highly recommended to prevent HBV/HCV co-infection among HIV-positive patients.

Key words: HIV/AIDS, hepatitis B (HBV) and C (HCV) viruses infection, co- infection, prevalence, correlation, Iran.

INTRODUCTION

Human immunodeficiency virus (HIV), hepatitis B virus (HBV) and hepatitis C virus (HCV) infections are among the grave health concerns confronting global health. Based on estimates from the UNAIDS (United Nations program on HIV/AIDS), 38.6 million people were living with HIV at the end of 2005 (Report on the Global AIDS Epidemic, 2006), three million having died from AIDS-related diseases. One third of these deaths were related to liver disorders caused by HBV/HCV co-infections (Kumarasamy et al., 2001; Rathi et al., 1997). These

infections spread via similar routes for example parenteral, sexual and vertical (Rathi et al., 1997) and therefore, high prevalence rates of HBV and HCV co-infections are anticipated in HIV infected patients (Kumarasamy et al., 2001; Rathi et al., 1997).

In HBV/HIV co-infected patients, HIV enhances HBV replication (Ramezani et al., 2011). This contention is still debatable, as the mechanistic details are not clear. In addition, HIV infection appears to increase the persistence of HCV infection and HCV RNA plasma level; however, the mechanism is still unclear (Ramezani et al., 2011). Progression of HCV-related liver disease towards end-stage, liver disease is accelerated in HIV/HCV co-infected patients (Ramezani et al., 2011; WHO, 2004; De Franchis et al., 2002; Andre, 2000). In the post-antiretroviral

*Corresponding author. E-mail: sahra_emamzadeh@yahoo.com. Tel: (+98) 021 66947984.

therapy (ART) era, HCV infection is becoming a major cause of premature death among people living with HIV/AIDS (Carmo et al., 2008; Low et al., 2008; Lo Re et al., 2008; Matthews and Dore, 2008).

HBV and HCV co-infections in HIV-positive patients lead to severe liver diseases by means of rapid progression to hepatocellular carcinoma and severe chronic hepatitis. In these co-infections, liver diseases are either caused by direct damage of hepatocytes via HBV or HCV infections (each of them or together) (Rathi et al., 1997), or by underlying conditions, such as alcoholism, injection drug use (IDU), sepsis, malnutrition or ART-related hepatotoxicity (Rathi et al., 1997).

Consequently, co-infection of these viruses is strongly associated with a reduced life span for HIV patients (Report on the Global AIDS Epidemic, 2006). In this manuscript, we identified HBV and HCV co-infection prevalence rates as it correlates in HIV-positive patients of Iran.

METHODOLOGY

The article was written on a systematic Medline search, Google scholar and SID (Scientific Information Database) using the below search terms: HIV, AIDS, HBV, HCV, co-infection, prevalence, etiology, risk factors, correlation, retro viral therapy, vaccination, injection and Iran. Related articles were ordered and referenced in this manuscript.

RESULTS

Prevalence

Various studies have been conducted among Iranian HIV-positive patients to identify HBV/HIV, HCV/HIV and HBV/HCV/HIV co-infection prevalence rates. These studies were performed in different cities and settings (for example, IDU patients, treatment centers, prisons, private clinics, hospital and community) throughout the country. HBV/HIV and HCV/HIV co-infections were assessed by measuring plasma markers such as HBs antigen, anti-hepatitis B core antigen and anti-hepatitis B surface antigen antibody for HBV/HIV co-infections and HCV RNA level, in addition to anti-HCV antibody, for HCV/HIV co-infections. Table 1 to 3 presents the results of co-infection studies conducted among Iranian HIV-infected patients.

Correlations

Different studies have found significant correlations between different types of risk factor exposure and HBV and/or HCV co-infection among HIV positive patients. In different studies, correlations were assessed between identified risk factors and co-infections. In most of the studies, IDU and unprotected sexual contact have been reported as the main risk factors for HCV/HIV and

HBV/HIV co-infections. These correlations are listed in Table 4.

DISCUSSION

In this study, we reported a wide spectrum of HBV and HCV co-infections among HIV-positive patients. Since HIV, HBV and HCV have similar routes of transmission many patients are infected with two or even all of these viruses (Puoti et al., 2002). A positive history of a blood transfusion, icteric appearance and dark-colored urine may suggest HIV/HCV co-infection; while a positive history of unprotected sexual contact, IDU and/or incarceration, in addition to icteric appearance and right upper quadrant (RUQ) tenderness in physical examinations, suggests HIV/HBV co-infection (Vahdani et al., 2009).

It is estimated that almost one third of HIV deaths are somehow associated with liver disease, which is mainly reported in the settings of co-infection with HBV/HCV. Extensive use of highly active anti-retroviral therapy (HAART) and the evident decline of opportunistic infections in HIV patients, has shed light on the morbidity and mortality attributed to HBV/HCV and end stage liver disease (Rathi et al., 1997).

Different prevalence rates of HBV/HCV co-infections among HIV-positive patients were reported in Iran and all over the world, which could be explained by the different epidemiology of these viruses in different regions of the country and the globe. The overlapping degree of various risk factors can determine the prevalence rate of HBV/HCV co-infection among HIV patients (Mohammadi et al., 2009). The mean co-infection rate of HCV/HIV, estimated 40% all across the world (Lazarus et al., 2007; Alter, 2006). It has also been reported that chronic HBV infection, as identified by the presence of the hepatitis B surface antigen, is found in 5 to 15% of HIV-infected patients globally (Ataei et al., 2010; Sulkowski, 2008; Lazarus et al., 2007; Alter, 2006).

Based on current estimates in Iran, the range of HBV/HIV co-infection varies from 9 to 44% (Badie et al., 2010; Sumathi et al., 2010; Adewole et al., 2009; Saravanan et al., 2007; Alter, 2006); however, HBV/HCV/HIV co-infection is estimated to be from 1 to 20% (Badie et al., 2010; Sumathi et al., 2010; Adewole et al., 2009; Alter, 2006). In a survey carried out in Ahvaz, a city south of Iran, the co-infection rates of HBV, HCV, and HBV/HCV in HIV patients was respectively 44%, 74% and 20% (Alavi and Etemadi, 2007).

Rates from a similar study conducted in the Lorestan province were 14.5% for HBV/HIV, 72% for HCV/HIV, and 7.9% for HBV/HCV/HIV co-infections (Mohammadi et al., 2009). A study conducted on 150 HIV positive patients from a private clinic in Tehran, identified HBV and HCV co-infection rates of 9.4 and 68%, respectively (Ramezani et al., 2006). In another Tehran study performed on 899 IDUs, HBV/HIV prevalence was reported

Table 1. Prevalence of HIV- HBV co-infections in different studies conducted in Iran.

Study	Setting of the study	Sample size ¹	No. of HIV+ patients	Prevalence of HBV-HIV co-infection (%)	Markers		
					HBs Ag (%)	Anti- HBs Ab (%)	Anti HbCAb (%)
SeyedAlinaghi et al., 2011	² PLWHA refer to Imam Khomeini Hospital, Tehran, Iran	201	201	89 (44.3)	27 (13.43)	23 (11.44)	60 (29.85)
Keramat et al., 2011	People refer to Behavioral counseling center, Hamadan, Iran	379	15	1 (0.3) ³	-	-	-
Ataei et al., 2010	PLWHA refer to a clinic in Isfahan, Iran	130	130	15 (11.5)	15 (11.5)	-	-
Mohammadi et al., 2009	PLWHA in the community, Lorestan province, Iran	391	391	57 (14.5)	57 (14.5)	-	-
Vahdani et al., 2009	Homeless men in the community, Tehran, Iran	202	13	10 (5) ³	-	-	-
Rahimi- Movaghar et al., 2010	IDUs from drug treatment centers and the community, Iran	864	90	67 (7.8) ³	-	-	-
Ramezani et al., 2006	Referred HIV-infected patients, Private clinic, Tehran, Iran	95	150	9 (9.4)	9 (9.4)	-	-
Mansoori et al., 2003	PLWHA refer to Masih Daneshvari Hospital, Tehran, Iran	39	39	25 (65)	8 (21)	17 (44)	-

¹Number of tested people. ²People living with HIV/AIDS. ³The measured markers were not differentiated exactly.

Table 2. Prevalence of HIV-HCV co-infections in different studies conducted in Iran.

Study	Setting of the study	Sample size ¹	No. of HIV+ patients	Prevalence of HCV ² -HIV co-infection (%)
SeyedAlinaghi et al., 2011	³ PLWHA refer to Imam Khomeini Hospital, Tehran, Iran	201	201	135 (67.2)
Keramat et al., 2011	People refer to Behavioral counseling center, Hamadan, Iran	379	15	13 (3.4)
Hosseini et al., 2010	Male IDUs at the temporary detention center, Tehran, Iran	417	112	100 (24)
Ataei et al., 2010	PLWHA refer to a clinic in Isfahan, Iran	130	130	100 (77)
Mohammadi et al., 2009	PLWHA in the community, Lorestan province, Iran	391	391	282 (72)
Vahdani et al., 2009	Homeless men in the community, Tehran, Iran	202	13	13 (6.4)
Rahimi- Movaghar et al., 2010	IDUs from drug treatment centers and the community, Iran	895	90	78 (8.7)
Ramezani et al., 2006	Referred HIV-infected patients, Private clinic, Tehran, Iran	95	150	65 (68)
Sharifi- Mood et al., 2006	PLWHA refer to Boo-Ali Hospital, Zahedan, Ira	52	52	6 (11.5)
Alavian et al., 2003	Hemophilic patients refer to Iran Hemophilia Society, Tehran, Iran	176	4	4 (2.3)
Mansoori et al., 2003	PLWHA refer to Masih Daneshvari Hospital, Tehran, Iran	44	44	36 (81)

¹Number of tested people. ²Based on anti-HCV antibody. ³People living with HIV/AIDS.

in 7.8% and HCV/ HIV prevalence was revealed in 8.7% of patients (Rahimi-Movaghar et al., 2010). Furthermore, in another study conducted in Isfahan, 11.5% of HIV patients were positive for HBs antigen, 77% were positive for anti- HCV

antibody and 9.2% were positive for both (Ataei et al., 2010). In another study in Zahedan, a city southeast of Iran, HCV/HIV co-infection rate was 11.5% (Sharifi-Mood and Metanat, 2010).

The considerably higher prevalence rate of

HCV/HIV co-infection compared to HBV/ HIV co-infection could be in part explained by the lack of an effective HCV vaccination program. Due to broad coverage of expanded programs of immunization (EPI), a considerable decline in

Table 3. Prevalence of HIV-HBV-HCV co-infections in different studies conducted in Iran.

Study	Setting of the study	Sample size ¹	No. of HIV+ patients	Prevalence of triple ² co-infection (%)
SeyedAlinaghi et al., 2011	³ PLWHA refer to Imam Khomeini Hospital, Tehran, Iran	201	201	73 (36.3%)
Keramat et al., 2011	People refer to Behavioral counseling center, Hamadan, Iran	379	15	1 (0.3)
Ataei et al., 2010	PLWHA refer to a clinic in Isfahan, Iran	130	130	12 (9.2)
Mohammadi et al., 2009	PLWHA in the community, Lorestan province, Iran	391	391	31 (7.9)
Vahdani et al., 2009	Homeless men in the community, Tehran, Iran	202	13	10 (5)
Rahimi- Movaghar et al., 2010	IDUs from drug treatment centers and the community, Iran	860	90	56 (6.5)
Hosseini Asl et al., 2004	Gypsies, Shahr-e-kord, Iran	226	4	1 (0.4)

¹Number of tested people. ²Based on HBs Antigen, Anti-HCV Antibody and Anti-HIV Antibody (all of them were positive). ³People Living with HIV/AIDS.

Table 4. Significant correlation of HBV and (or) HCV co-infection among HIV positive patient in different studies conducted in Iran.

Study	Co-infection	Significant correlations*
SeyedAlinaghi et al., 2011	HIV-HBV-HCV	Male gender (p<0.0001) Route of transmission: IDU (p<0.0001), unsafe sex (p<0.0001), more than one risk factor (p<0.003)
Badie et al., 2010	HIV-HBV-HCV	Male gender (p=0.007) Age>60y (p=0.002) IDU (p=0.000) (most important risk factor)
Ataei et al., 2010	HIV-HCV	Low education History of imprisonment (p=0.000) Young age Being single (p=0.02) High-risk sex (p=0.002) IDU (p=0.000) (most important risk factor)
Sharifi-mood et al. 2010	HIV-HCV	Route of transmission: IDU
Mohammadi et al., 2009	HIV-HBV-HCV	Gender (p<0.001): Male for HIV-HCV, Female for HIV-HBV, Female for HIV-HBV-HCV Age (p<0.001): <40y for HIV-HCV, 31-50y for HIV-HBV-HCV Occupation (p<0.001): Unemployed patients for HIV-HCV, ranchers /farmers/ housewives for HIV-HBV, housewives for HIV-HBV-HCV Marital status (p<0.001): Single for HIV-HCV, married for HIV-HBV, married for HIV-HBV-HCV Route of transmission: Blood transfusion and IDU for HIV-HCV, pregnancy and having infected family members for HIV-HBV, unsafe sex and IDU for HIV-HBV-HCV

Table 4. Contd.

Vahdani et al., 2009	HIV-HCV and HBV	HIV-	Route of transmission: IDU for HIV-HBV ($p < 0.02$), IDU for HIV-HCV ($p < 0.0003$) History of imprisonment ($p < 0.05$)
Rahimi-movaghar et al., 2008	HIV-HCV		Route of transmission: IDU ($p < 0.001$)
Hosseini Asl et al., 2004	HIV-HCV		Route of transmission: History of blood transfusion, tattooing, phlebotomy
Mansoori et al., 2003	HIV-HCV		Route of transmission: IDU

*, P-values are presented in parentheses.

HBV infection has been achieved throughout the general public; therefore, higher rates of HBV infection would be anticipated among groups with high risk behaviors. Additionally, sexual transmission of HCV is lower in comparison to HBV and it is mostly transmitted via IDU (SeyedAlinaghi et al., 2011). Since a majority of Iranian HIV-positive patients have contracted HIV through IDU, HCV co-infection has a high prevalence among these patients (SeyedAlinaghi et al., 2011). Moreover, different laboratory indicators were measured to assess HBV infection in various studies: Some studies have identified HBV/HIV co-infection rate by assessing HBs antigen plasma level, while other studies have evaluated anti-HBs or anti-HBc antibody plasma levels (SeyedAlinaghi et al., 2011). In one survey in Tehran, HBV/HIV co-infection was measured by measuring three HBV markers. In this study, the prevalence rates for HBs antigen, anti-HBc and anti-HBs were 13.4, 29.8 and 11.4%, respectively (SeyedAlinaghi et al., 2011).

Several factors have been associated with the increased risk of HBV/HCV co-infection among HIV patients. A study in Isfahan revealed that illiteracy, a low educational level, positive history of incarceration and young age are associated with an increased risk of HIV/HCV co-infection. Incarcerated HIV-positive patients are more likely

to share needles, as well as razors and tattooing equipment. In this study, low education and young age were significantly associated with an increased rate of HCV/HIV co-infection, which may be due to the practice of high risk behaviors and the lower level of knowledge in young and less-educated adults (Ataei et al., 2010). A recent study has shown that the main route for HCV/ HIV transmission among monogamous couples was through IDU (SeyedAlinaghi et al., 2011). Additionally, several studies reported that male gender is associated with a significantly higher risk of HBV/ HIV co-infection (SeyedAlinaghi et al., 2011; Gupta and Singh, 2006; Alter, 2006).

RECOMMENDATIONS AND CONCLUSIONS

In this review, we reported the results of surveillance studies conducted to identify HIV and HBV/HCV co-infection rates in Iran. Based on these studies it was identified that a majority of Iranian co-infected patients are men. Older HIV patients were more likely than younger patients to be co-infected.

In these studies IDU and sexual routes were shown to be the most prevalent routes of transmission. Moreover, HBV vaccination seems to significantly decrease the risk of co-infection

(Vahdani et al., 2009).

The timely diagnosis of concurrent HBV/HCV infections in HIV patients is of great value and requires a detailed history of the patient's life, as well as a physical examination. Generally, the common risk factors associated with HBV/HCV co-infection among HIV patients are tattoos (especially in prison), IDU, history of incarceration and history of other sexually transmitted infections (STI).

Frequently performed liver function tests (LFT) and drug plasma level measurements are of great significance when it comes to the timely detection of hepatocyte damage in co-infected patients. Routine neonatal HBV vaccination, as well as HBV vaccination in high risk groups (e.g. health care workers) has lowered HBV infection prevalence in Iran (Alavian et al., 2007; Zamani et al., 2006). Therefore, HBV vaccination should be considered as the cornerstone of preventive strategies among HIV-positive groups in which high risk behaviors are routinely practiced. Although IDU HIV-positive patients would benefit best from harm reduction and needle exchange programs, the exact efficacy of these interventions in preventing HBV/HCV infections have been less identified. To further increase patient survival, access to HAART for co-infected patients should also be extended via implementation of effective

governmental policies in a global level (Badie et al., 2010).

The alarming high rate of HBV/HCV co-infection among HIV patients highlights the need for a timely and systematic assessment of these patients. It is evident that early diagnosis and initiation of appropriate treatments could increase their survival; therefore a comprehensive identification of risk factors and underlying conditions, as well as HIV treatment and frequently performed laboratory tests, are highly recommended to prevent HBV/HCV co-infection in these patients (Puoti et al., 2006; Vallet-Pichard and Pol, 2006; Herrero, 2001; Scharschmidt et al., 1992).

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