



Prevalence of Hepatitis B Co-Infection among HIV Positive Patients: Narrative Review Article

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Abstract

Background: Hepatitis B virus (HBV) is the most prevalent viral infection and is among the leading causes of human liver diseases. Nearly 360 millions of people are world widely infected with prolonged forms of hepatitis B including active and inactive chronic forms. Chronic hepatitis B (CHB) is associated with cirrhosis and hepatocellular carcinoma (HCC) in patients suffering from congenital and/or acquired immunodeficiency and also following immunosuppressive therapy. The target cell of human acquired immunodeficiency virus (HIV) is CD4 positive T cells. These cells play central role(s) in both cellular and humoral immunity so that the HIV attack of CD4 positive T cells causes suppression of both cell-mediated and humoral immune responses. One of the frequent complications in HIV positive patients is HBV co-infection and as a result, the co-transmission of these viral diseases is common. Due to the paramount importance of the co-infection of HBV and HIV, it is noteworthy to investigate the prevalence of hepatitis B in these patients for planning of an effective therapeutic strategy. Based on these considerations, the main aim of this review article was to collect and analyze the recent and relevant studies regarding the prevalence rate of hepatitis B co-infection among HIV positive patients world widely.

Keywords: HIV, Chronic hepatitis B infection, Co-infection

Introduction

Hepatitis B virus (HBV) is the most important and prevalent infectious agent leading to inflammation of human liver (1, 2). Recent reports stated that 360 millions of people are globally suffering from the chronic forms of HBV infection (CHB) (3). It has been documented that prolonged forms of hepatitis B, including active and in-active CHB, can be considered as major candidates for induction of several complications such as hepatocellular carcinomas (HCC) and cirrhosis (4). In addition to HCC and cirrhosis development, hepatitis B infection is also able to develop active and acute forms of HBV infection in congenital and/or ac-

quired immunodeficiency and also following immunosuppressive therapy (5). Human acquired immunodeficiency virus (HIV) attacks CD4⁺T cells, as critical cells in both cellular and humoral immunity, leading to defective cell-mediated and humoral immune responses (6, 7) and predisposing patients to future infectious diseases (7).

It has been documented that one of the frequent complications of HIV infection is hepatitis B co-infection and due to the common methods of transmission of these two viruses, the incidence rate of co-infection is increasing (8). It has been established that following reduction in the CD4

positive cells count to lower than 200 cells/ml, the immune system of HIV positive patients fails to develop an adequate immune response against microbial agents and as a result re-activation of HBV infection and its related complications will occur (9).

Due to the vital aspects of this co-infection, the present study was conducted to investigate the prevalence of this condition in the hope that more effective therapeutic plans for patients are developed.

Methods

The presented data in this review was obtained by searching the HIV, HBV, hepatitis B and co-infection as key words in PubMed, Google Scholar and SCOPUS databases. All the publications which had evaluated HBV co-infection with HIV were included to the current review article. The data which have presented in patients suffering from co-infection with other infectious diseases have excluded from the review article. There was no date limitation for the included studies.

Worldwide prevalence of HIV-HBV co-infection

Several studies are performed in the field of HIV-HBV co-infection worldwide as follows (Table 1).

HIV-HBV co-infection in European countries

The co-infection of HIV-HBV has been well investigated in European countries. Several studies have been established that the prevalence of HIV in European countries is lower than others especially African and Asian countries. 15.4% (27 cases) out of 175 HIV positive Italian patients were co-infected with HBV (10). A study in the Netherlands identified that 3.6% of HIV-infected patients were HBsAg positive (11). In Germany reported among 232 HIV-infected patients 9.48% of cases suffered from CHB (12). In France, investigators indicated that 45% of 383 HIV positive patients had detectable HBV-DNA (13, 14), while, isolated anti-HBC antibodies was positive in only 12% of patients (13, 14). A study on 166

French HIV positive patients revealed that 7.8% of patients had also HBV infection (15). A similar study in this country indicated that the frequency of occult hepatitis B infection (OBI) in HIV-infected patients was 5.4% (16). Another investigation on 508 Spanish HIV positive patients and revealed that 4.7 percent of the patients had OBI/HIV co-infection (17). Interestingly, Nikolopoulos et al., using a larger sample size of 1729 cases of HIV positive Greece patients, displayed that 6% of these patients were positive for HBV co-infection (18). In western and central European countries as well as in Ukraine, 1050 HIV-infected women were enrolled in the European collaborative study and the results demonstrated that 4.9% of the subjects were HBsAg positive (19).

Based on the results of the relevant studies conducted in the European countries, it can be inferred that although the rate of hepatitis B is comparatively low, the frequency of HBV co-infection is partially high in HIV positive patients.

HBV Co-infection in Asian HIV positive patients

HBV infection is endemic in Asia especially in south-eastern parts (20). Although the number of studies is limited, a relatively high prevalence of co-infection has been reported in Iran. For instance, in a population of 899 of Iranian injecting drug abusers, 7.8% were co-infected by HIV, HBV and also HCV (21). Another study on Iranian population revealed that 28.6% of HIV positive individuals were infected with HBV (22). There is another report showing that the HIV co-infection in HBV positive patients is 1.8% among 168 HBV positive patients (23). The rates of 14.5 and 11.25 % of HBV co-infection have been demonstrated in Iranian HIV positive patients (24, 25).. In China as endemic area for hepatitis B, 29.34% of 92 HIV positive individuals were co-infected with OBI form (26). Moreover, another study from China showed that among 395 HIV positive patients, 6.07 percent were co-infected with HBV (27). Interestingly, a same study by Japanese researchers showed that among 394 HIV infected homosexual men, 7.9% cases were posi-

tive for HBsAg (28). Additionally, another study on Japanese HIV positive patients identified that 11.9% and 3.2% were also infected with HBV (29, 30). Studies from India demonstrated that 9, 10.7, 7.28 and 13.7 % of HIV positive patients had suffered from HBV co-infection (31-34). Also, finding of a study on 874 HIV-infected patients in India indicated that 8.35 percent of them were infected with HBV (35). Based on the aforementioned studies which performed in Asian countries, it appears that the rate of HIV/HBV co-infection is lower than European countries. The plausible reasons to explain why the rate of HIV/HBV co-infection is higher in European than Asian countries, are discussed in next sections.

HIV/HBV co-infection among American countries

America is known as the continent with the least HBV prevalence but the HIV-HBV co-infection is frequent in America as well (36). A study from Atlanta which carried out on a big HIV infected population (2818 cases) showed that 59.8% of cases had HBV co-infection (37). In Canadian HIV positive patients, it has been evidenced that 10.46 percent of 1223 patients were also co-infected with HBV (38). The prevalence of hepatitis B infection among 5639 cases of HIV positive in New York city has been reported as 4.47% (39). Interestingly, another large population revealed that 4.6% out of 4721 HIV infected patients were co-infected with HBV (40). An investigation on 401 Brazilian HIV infected patients demonstrated that the overall prevalence of hepatitis B markers was 40.9%, with 8.5% for HBsAg, 39.7% for total anti-HBcAg and 5.5% for anti-HBsAg (41). Another study showed that the prevalence of hepatitis B in a sample of 406 Brazilian adult patients with HIV infection was 51% for HBsAg, 45.1% for anti-HBc and 32.3% for anti-HBs (42). It has also been reported that the prevalence of anti-HBc and HBsAg were 40% and 3.7% of, respectively, in HIV positive patients (43). Interestingly, high prevalence of HBV infection among HIV patients were also reported (44). The study displayed 30.4% of HIV positive patients were co-infected with HBV (44). Based on the aforemen-

tioned studies, although the prevalence rate of co-infection in European and American is comparatively lower, American population has a higher prevalence of co-infection.

Epidemiology of HBV co-infection among African HIV infected patients

Previous studies demonstrated that sub-Saharan Africa is highly endemic for HBV and HIV infections (45). Hence, it seems that HBV infection is also prevalent in African HIV positive patients. Recent studies confirmed this hypothesis. For instance, a study revealed that 12.17% out of 115 pregnant HIV positive women in Borkinafaso were infected with HBV (46). HIV-HBV co-infection was also reported in Mali by evaluation of a large sample size of 11592 blood donors. This study identified that the prevalence of HIV and HBV were 4.5% and 14.9%, respectively, while the prevalence of HIV/HBV co-infection was only 1.13% in this population (47). Investigators in Abidjan (eastern part of Africa) also showed HIV/HBV co-infection in 9.01% individuals of 499 pregnant women (48). 21% of Cameroon HIV positive patients were also infected with HBV (49). Another study from sub-Saharan Africa which carried out on 200 HIV positive patients revealed that the HBV co-infection was prevalent in 10% of evaluated patients (45). Lodenyo and colleagues identified that 3% of HIV positive patients were diagnosed as HIV/HBV co-infected individuals (50). High levels of HBV/HIV co-infection were also reported from South Africa (51). The study identified that 20% of 537 HIV infected individuals were HBsAg positive (51). Another study from Nigeria on a large sample of HIV-infected patients, total of 1779, identified that HBsAg was present in 11.9% of cases (52). Interestingly, their results demonstrated that HBsAg was more common among males than females (52). High levels of HIV/HBV co-infection from Nigeria also was reported by researchers (53). Their results showed that HBsAg was detectable in 28.4% of 102 HIV infected patients (53). Interestingly, it has been demonstrated that 9.7% of 342 HIV positive Nigerian patients has suffered from HIV/HBV co-infection (54). Also a study on 401 Nigeria HIV positive pregnant women revealed that 6.5% of

them had HBV co-infection (55). According to the presented studies, it seems that the rate of HIV/HBV in the African countries is the same as

Asian countries and is lower than of the American and European countries.

Table 1: A summary of the literature reviewed in HIV positive patients

Diseases	Country	Racial Information	Sample size	Percent of HBV/HIV co-infection	Ref.
Europe	Italy	Italian	175	15.4	(13)
	Spain	Spanish	508	4.7	(21)
	Germany	Germany	232	9.4	(15)
	Finland	Finland	22	59.0	(16)
	France	French	383	45.0	(18)
	France	French	111	5.4	(20)
	France	French	166	7.8	(19)
	Netherlands	Netherlands	-	3.6	(14)
	Greece	Greeks	1729	6	(22)
	Asia	Iran	Iranian	391	14.5
Iran		Iranian	80	11.3	(29)
Iran		Iranian	899	7.8	(25)
Iran		Iranian	-	28.6	(26)
Iran		Iranian	168	1.8	(72)
China		Chinese	395	6.1	(31)
China		Chinese	92	27	(30)
India		Hindi	58	13.7	(38)
Japan		Japanese	394	7.9	(73)
Japan		Japanese	700	11.9	(33)
Japan		Japanese	126	3.2	(34)
India		Hindi	500	9.0	(35)
India		Hindi	837	7.28	(37)
India		Hindi	874	8.3	(39)
India		Hindi	112	10.7	(36)
America	Australia	Australian	537	20.0	(55)
	Canada	Canadian	1223	10.46	(42)
	Canada	Canadian	1050	4.9	(23)
	Cameron	Cameroonian	159	21.0	(53)
	America	American	2818	59.8	(41)
	America	American	5639	4.47	(43)
	America	American	4721	4.6	(44)
	Cuba	Cuba	325	30.4	(74)
	Brazil	Brazilian	401	8.5	(45)
	Brazil	Brazilian	406	7.9	(46)
Africa	Brazil	Brazilian	1000	3.7	(47)
	Nigeria	Nigerian	1779	11.9	(56)
	Nigeria	Nigerian	102	28.4	(18)
	Nigeria	Nigerian	342	9.7	(58)
	Nigeria	Nigerian	401	6.5	(59)
	Borkina faso	Burkinan	115	12.17	(50)
	Ivory Coast	Ivory Costian	499	9.0	(52)
	Africa	African	200	10.0	(49)
Africa	African	100	3.0	(54)	
Mali	Malian	11592	1.13	(51)	

Discussion

Based on the aforementioned studies, it seems that the prevalence of HBV co-infection among HIV positive patients are 3.7 to 59.8, 3.6-59, 1.8-28.6 and 1.1-28.4 percent in the American, European, Asian and African countries, respectively. According to this information, it can be concluded that, although, Africa (56, 57) and Asia (58, 59) are endemic areas for HIV, but the incidence of HIV/HBV co-infection is higher in the American and European populations. It appears that several mechanisms may be responsible for this higher rate of co-infection as follows; 1. American and European countries employ excremental techniques with a higher sensitivity enabling them to detect the minimum rate of co-infection. 2. The sample size of studies conducted in these countries was larger than the African countries. 3. Previous studies demonstrated that American and European populations carrying CCR5 delta 32 mutation in more than 15% of individuals which leads to protection from HIV infection (60, 61). Since the HBV infection rate is the same as Asian and African countries, it has increased the chance of HIV/HBV co-infection. 4. While, the mode of transmission for these two viral infections can be various in Asian and African countries, in American and European countries, these infections are mostly transmitted sexually (62-67).

Conclusion

HIV-HBV co-infection is worldwide frequent. According to the findings of this study, the incidence of HIV/HBV co-infection in the American and European countries are higher than the Asian and African population which may attract more attention in this regard. Finally, the higher prevalence of HBV in HIV positive patients may be ascribed to the suppression of immune responses in HIV positive patients against HBV infection rather than to the other background reasons. Further studies and attention are warranted in this aspect for planning of more effective prophylactic or therapeutic strategies.

Ethical considerations

Ethical issues (Including plagiarism, Informed Consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc.) have been completely observed by the authors.

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