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**Viral hepatitis and human immunodeficiency virus co-infections in Asia**

Utsumi T *et al.* Viral hepatitis and HIV co-infection

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**Abstract**

Hepatitis B virus (HBV), hepatitis C virus (HCV), and human immunodeficiency virus (HIV) affect many people in Asian countries, although there are geographic differences. Both HBV and HIV (HBV/HIV) and HCV/HIV co-infections are highly prevalent in Asia. Hetero- and homosexual, injection drug use, and geographic area are strong predictors of HBV, HCV, and HIV serostatus. In HBV endemic regions, the prevalence and genotype distribution of HBV/HIV co-infection is almost comparable with that in the general population. In Japan, where HBV has low endemicity, the prevalence of HBV/HIV co-infection is approximately 10-fold higher than that in the general population, and HBV Ae is the most common subgenotype among HIV infected individuals. Highly active antiretroviral therapy (HAART) is an effective treatment for HIV/Acquired Immune Deficiency Syndrome. Lamivudine, a component of HAART, is an effective treatment for HBV, HIV, and HBV/HIV co-infection; however, cost, emerging drug resistance, antiretroviral-associated liver toxicity and liver-related morbidity due to HCV progression are particular concerns. HCV/HIV co-infection may accelerate the clinical progression of both HCV and HIV. The high prevalence of HBV/HIV and HCV/HIV co-infections in Asia underscores the need to improve prevention and control measures, as fewer evidence-based prevention strategies are available (compared with Western countries). In this review, the most recent publications on the prevalence of HBV/HIV and HCV/HIV co-infections and related issues, such as therapy and problems in Asia, are updated and summarized.

**Key words:** Hepatitis B virus; Hepatitis C virus; HIV; Co-infection; Prevalence; Asia; Pathogenicity; Drug resistance; Natural history; Problems

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**Core tip:** Hepatitis B virus (HBV) and hepatitis C virus (HCV), infections are common among human immunodeficiency virus (HIV) positive individuals due to similar blood-borne transmission routes. Highly active Highly active antiretroviral therapy is an effective treatment for HIV/Acquired Immune Deficiency Syndrome; however, emerging drug-resistant viruses and drug-induced hepatotoxicity are particular concerns. The high prevalence of HBV/HIV and HCV/HIV co-infections in Asia highlights the need to improve prevention and control measures because, unlike in Western countries, few evidence-based prevention strategies are available. Here, we review the epidemiologically and clinically important aspects of HBV/HIV and HCV/HIV co-infections in Asian countries.

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**INTRODUCTION**

An estimated 240 million people worldwide are chronically infected with hepatitis B (HBV), and 170 and 34 million people are infected with HCV and human immunodeficiency virus (HIV), respectively[1]. Although the prevalence of these viral infections varies according to geographic region, the majority of cases occur in developing Asian and African countries[2,3]. Co-infection with HBV or HCV is common among HIV-positive patients due to their similar blood-borne transmission routes (*e.g.*, sexual and perinatal for HBV[4], and percutaneous for HCV).

HIV co-infection has a deleterious effect on the outcome of patients with chronic viral hepatitis and greatly complicates their management. HIV-positive individuals with chronic hepatitis (caused by either HBV or HCV) have greater liver mortality than those infected with HIV alone. Moreover, the highest reported mortality is among those with multiple hepatitis infections[5]. Although the burden of HBV and HCV infection is greatest in Asia, the biological characteristics associated with either HBV or HCV infection among HIV-infected individuals are unclear. YMDD motif mutants in HBV and occult hepatitis virus infection were observed in Asia[6] and these were found to be related to severe liver diseases and resistance to treatment and prevention[7]. This article provides an overview of the epidemiology of hepatitis B and C virus infections among HIV-infected individuals in Asian countries.

**HIV EPIDEMIOLOGY IN ASIA**

In the early-to-mid 1980s, much of the world was dealing with serious [HIV](http://www.avert.org/hiv.htm" \t "_self) and [AIDS](http://www.avert.org/aids.htm" \t "_self) epidemics, although Asia remained relatively unaffected. However, by the early 1990s, AIDS epidemics had emerged in several Asian countries and, by the end of the decade, had spread rapidly across the continent. Today, almost 5 million people in South, East, and Southeast Asia are infected with HIV. The epidemiology of the disease in different Asian countries is unique. In fact, the epidemiology can be different among areas/districts/provinces within the same country. By 2010, between 3.0 and 3.9 million people in Southeast Asia were living with HIV/AIDS, which was up from 3.3 million in 2009. Women account for 37% of those infected, the majority of whom were infected by a partner. However, the HIV epidemic in Southeast Asia is now declining: the number of new infections has fallen by 34% (from 320000 in 2001 to 210000 in 2010). According to the Joint United Nations Program on the global HIV/AIDS (UNAIDS) epidemic, 2011, Southeast Asia recorded above-average declines in the number of new HIV infections[8]. The WHO Southeast Asia Region (SEAR) comprises 11 countries: Bangladesh, Bhutan, South Korea, India, Indonesia, the Maldives, Myanmar, Nepal, Sri Lanka, Thailand, and Timor-Leste. The region has a combined population of over 1.8 billion. Five countries (India, Indonesia, Myanmar, Nepal and Thailand) account for the majority (99%) of HIV cases. India has the second highest HIV burden of any country in the world. There are few reports of HIV cases in Korea, Bangladesh, Bhutan, the Maldives, Sri Lanka, or Timor-Leste, which together represent less than 1% of all HIV infections recorded in the SEAR. The annual number of new infections reported in four of the five countries with a high HIV burden (namely India, Myanmar, Nepal, and Thailand) is declining. However, the number of cases in Indonesia continues to rise, making the epidemic in this country one of the fastest growing in Asia[9,10].

**HBV/HIV CO-INFECTION IN ASIA**

***Epidemiology and risk factors***

Approximately 240 million people are chronically infected with HBV, approximately 600000 of whom die each year of HBV-related diseases or hepatocellular carcinoma (HCC)[11]. Although the global prevalence of HBV varies from region to region, approximately 5%-10% of HIV-infected individuals are chronically infected, which is defined as persistent detection of hepatitis B surface antigen (HBsAg) for more than 6 months. In areas with a low HBV prevalence (< 2% of individuals are HBsAg-positive), such as Western countries and Japan, chronic HBV infection among HIV-positive individuals is approximately 10-fold higher than that in the general population[12]. On the other hand, the prevalence of HBV infection in some parts of Africa and Asia is approximately 10%-15%, regardless of HIV co-infection[13].

The major route of HBV infection, especially in HBV endemic regions, is mother-to-child transmission. In HBV endemic regions, the prevalence and genotype distribution of HBV in HIV-infected patients is comparable with that in the general population[6,14]. Table 1 shows the prevalence of HBsAg and lists the risk factors and major HBV genotypes identified in HIV-infected individuals in Asia. Japan is the only country with low endemicity of HBV infection in Asia[7]; however, it is 10 times more prevalent among HIV-infected individuals. A higher prevalence of HBV/HIV co-infection compared with the prevalence of HBV infection alone is observed in Indonesia, Vietnam, and India. Interestingly, Ae (HBV/Ae), which originated in Europe and the United States, is the most common HBV genotype in HBV/HIV co-infected patients in Japan, even though HBV/B and HBV/C are indigenous[15]. An individual infected with HBV/Ae (as opposed to other HBV genotypes) is at a higher risk of co-infection with HIV.Furthermore, HBV/Ae (which tends to be chronic)[16] is detected almost exclusively in homosexual men[16-18]. Indeed, in Myanmar, homosexual men carry the greatest risk of being co-infected with HBV and HIV[19], and an increased prevalence of HBV/HIV infection is also observed in men with a history of IDU[20]. A substantial number of HBV-infected individuals in Indonesia, Vietnam, Thailand, and India are also infected with HIV (15.3%, 28.0%, 13.0% and 11.3%, respectively)[6,20,21-25]. Indonesia is currently experiencing an increasing HIV incidence and a high HBV burden[6,19,24]; however, no HBV/HIV co-infection cases have been identified in commercial sex workers (CSW)[25]. In Thailand, HBV/HIV co-infection is more common in HIV-infected adolescents who are negative for anti-HBV antibodies[26]. HBV/HIV co-infection is also common in China, where sexual transmission is an independent risk factor, followed by ethnicity and occupation[27]. Additionally, the incidence of co-infection among HIV-infected children receiving antiretroviral therapy (ART) is high. Significant levels of co-infection by blood-borne viruses are observed among IDUs and CSWs in Vietnam[22]. The main risk factor for HBV/HIV co-infection in India is heterosexual sex, whereas it is homosexual sex and IDU in other Asian countries.

***Treatment and drug resistance***

Several of the antiretroviral drugs used to treat HIV infection can also be used to treat HBV infection; therefore, they can be used to treat some co-infected patients[37]. On the other hand, HBV/HIV co-infection may complicate the delivery of ART by increasing the risk of drug-related hepatotoxicity and impacting the selection of specific agents, such as drugs that are effective against both HBV and HIV[34].

Lamivudine, a component of highly active antiretroviral therapy (HAART), is used widely because it is easy to obtain, relatively cheap, and its clinical efficacy has been shown in long-term follow-up studies[35-37]. However, lamivudine often induces mutations within the RT domain of the viral polymerase region, resulting in multidrug-resistance and a poor prognoses for some HBV/HIV co-infected individuals. Table 2 shows the effects of ART on HBV/HIV co-infection and drug resistance in Asian countries. Because lamivudine is associated with the emergence of drug-resistant strains, the current recommended treatment for co-infected individuals is a tenofovir (TDF)-based regimen[38]. Drug-resistant mutations, particularly multidrug-resistant mutations, are the major concern for patients receiving long-term therapy with nucleoside analogues (NA), such as lamivudine[7]. A high prevalence of lamivudine-resistant mutation has been reported in adolescents from Thailand (M204V/I)[26], Vietnam (L180M and M204V)[13], and Indonesia (M204I and M204I + L180M)[6]. However, V173L + L180M + M204V was identified in HBV/HIV co-infected patients who were not treated with lamivudine[16]; L217R, M184V, and I195M were identified in lamivudine-treated patients[39] in Japan; and L180M and M204V were identified in ART-naïve patients in India[23]. One study suggests that all patients should be screened for HBV prior to ART initiation, as this would enable the most appropriate regimen to be selected[26]. Combination treatment with TDF plus either emtricitabine or lamivudine is recommended for patients who are co-infected with HBV/HIV[40]. However, many countries/regions are experiencing difficulty in accessing effective drugs (even the drugs recommended in their own guidelines) due to the lack of availability and/or high cost. Moreover, some developing Asian countries/regions lack experienced hepatologists and HIV specialists who can manage HBV, HIV, and HBV/HIV co-infection effectively.

Antiretroviral-associated liver toxicity [due to use of nevirapine (NVP) use] was reported in both Thailand and Indonesia, and in some cases, ART with lamivudine did not suppress HBV[6,21]. In Vietnam, the precore mutation, G1896A, which is highly associated with HCC, is more common in HBV/HIV co-infected individuals harboring the HBV genotype B (HBV/B) than in those harboring HBV/C[22]. HBV replication can occur in the absence of HBsAg (known as occult HBV [OHBV] infection). OHBV has been reported in HIV-infected individuals, although the underlying mechanisms are unclear[6,41]. The majority of perinatally infected HIV-positive adolescents in Thailand do not produce HBV protective antibodies, even though hepatitis B vaccination coverage is high. Thus, the HBV seroprotection level is low despite childhood vaccination, suggesting that the populations at risk for HBV infection require a booster dose of an HBV vaccine[26]. The current recommendation in Japan is that all newborn babies are vaccinated against hepatitis B.

**HCV/HIV CO-INFECTION IN ASIA**

***Epidemiology***

HCV and HIV are among the top ten leading causes of death due to infectious disease worldwide. HCV accounts for an estimated 170 million chronic infections and HIV accounts for approximately 34 million infections[1]. These viruses, together with HBV, share transmission routes, although their prevalence differs according to the transmission efficiency and geographic region[4].

The overall prevalence of HCV/HIV co-infection ranges from 1.2% to 98.5% in South and Southeast Asia[45]. These estimates are influenced by several factors, including geographic differences in the prevalence of chronic infection in different age groups, transmission efficiency *via* certain routes, and the number of individuals at high risk for infection[4].The HCV transmission risk is significantly higher among patients who acquired HIV infection via the parenteral route rather than the sexual route. Although the sexual route is a common mode of HIV transmission, it is less common for HCV[46]. Today approximately one-quarter of HIV-infected individuals in Europe and the USA are co-infected with HCV[47]. HCV infection outbreaks have been reported in HIV-positive men who have sex with men (MSM) in North America, Europe, and Asia. Transmission is believed to be the result of exposure to blood during sexual contact[48]. HCV-RNA was detected in 38.2% of anti‑HCV‑negative samples in Indonesia[10]. Sexual contact is still the main HIV transmission route in Indonesia, whereas HCV is less easily transmitted via the sexual route. Thus, among the heterosexual transmission history, the HCV‑seropositive rate (26.9%) was significantly higher compared with the HCV infection rate alone, which may be due to the HCV transmission mechanisms between sexual partners, particularly those who engage in practices that are associated with a high virus transmission risk[10]. Sulkovski *et al*[49] and others also reported HCV infection with sexual transmission between HIV-infected MSM and other individuals with abnormal sexual activities[49]. The European AIDS Clinical Society guidelines on co‑infection suggest that patients who are beginning HIV therapy should be serologically tested for HCV. It also suggests that HCV RNA-negative and anti-HCV antibody‑negative patients exhibiting an unexplained increase in alanine transaminase levels, and those at high risk for HCV infection (*e.g.*, IDU and those likely to suffer mucosal trauma during intercourse) should be tested annually thereafter[46].

A study regarding HIV and HCV infection among those receiving methadone maintenance treatment (MMT) in clinics in Yunnan, China, showed that the prevalence of HIV seropositivity in rural and urban areas was 27.7% and 10.0%, respectively, and the prevalence of HCV seropositivity was 75.6% and 46%, respectively; however, the prevalence of HIV/HCV co-infection was 20% and 7%, respectively. Over three-quarters (76.2%) of the HIV-infected participants in this study were also infected with HCV[50]. The majority of heroin is smuggled into Yunnan province from Myanmar. It then moves along drug trafficking routes to other areas of the country. Thus, high levels of illicit drug use and HIV and HCV epidemics are common in Yunnan[51-53]. Urban and rural MMT patients know little about HIV and HCV; therefore, education programs in MMT clinics must be improved. Studies performed in Beijing, Henan, Guangxi, Kunming, Sichuan, Hunan, Xinjiang, and Shanxi reveal that the prevalence of HCV co-infection among HIV-infected individuals ranges from 11.6% to 85.0%, depending on the area surveyed. The primary transmission route favored by each of these viruses may explain these differences. The co-infection rates in IDUs (58.2%-91.6%) and commercial blood donors (15.8%-71.6%) are significantly higher than those in individuals who become co-infected via sex (5.3%-20.0%)[54]. Another study from Central China shows that only 62.4% of HIV-infected individuals have anti-HCV antibodies[30]. In Vietnam, 89.8%-98.5% of HIV-positive IDUs are infected with HCV. A study in southern India found that 18 (15%) and 10 (8.3%) out of 120 HIV-infected patients were also positive for HBsAg and anti-HCV antibodies, respectively. The study, which was carried out in a tertiary care center, also found that the most common transmission routes were sexual promiscuity (79%), followed by sex with a positive spouse (15%), and a blood transfusion history (6%)[55]. A cross-sectional study performed in Mazandaran province, Iran, from 2008 to 2010 showed that of 80 HIV-positive patients, only 33.8% were co-infected with HCV, whereas 25% were co-infected with both HBV and HCV. Thus, 58.8% of HIV-positive patients were also infected with HCV[56]. A study of 33255 blood samples from in Kathmandu, Nepal, reported that the HIV seroprevalence was 0.19% and that 10.8% of the donors were co-infected with HCV[57]. Additionally, the study found similar HIV seroprevalence rates between first-time and repeat donors, and between volunteer and replacement donors, indicating the need for more effective donor recruitment, education, and counseling strategies.

***Natural history***

HCV and HIV co-infection enhances liver damage and increases the risk of developing end-stage liver disease and HCC. From a clinical perspective, HCV/HIV co-infection is the most common cause of liver cirrhosis in these patients; therefore, monitoring and treatment of these infections must be prioritized, even though this is more difficult to achieve than in HCV-monoinfected individuals[58,59]. A meta-analysis that examined the impact of HIV infection on HCV-infected individuals revealed that HCV/HIV co-infection was associated with a 6.14-fold increase in the relative risk for end-stage liver disease and a 2.07-fold increase in the relative risk for cirrhosis compared with HCV mono-infection[60,61]. On the other hand, HCV/HIV co-infected patients respond less well to antiviral therapy with peginterferon + ribavirin (pegIFN + RBV), resulting in a lower sustained virological response (SVR) after antiviral therapy. HIV/HCV co-infected individuals develop end-stage liver disease more quickly than either HIV- or HCV-monoinfected patients[30,55], particularly those receiving long-term immunosuppressive regimens. Thus, early HCV/HIV co-infection diagnosis may allow for prompt co-morbidity recognition of and prevent future complications.

***Problems***

Unsafe therapeutic injections performed by both professionals and non-professionals appear to be the predominant HCV transmission mode in countries/regions with moderate-to-high prevalence; indeed, such cases account for up to 40% of all HCV infections worldwide. The predominant transmission mode in most low prevalence areas is IDU[4,62-64]. Although transfusion- and transplant-associated HCV infections are minimized by routine testing of donors, and preventing a new generation of young injectors from becoming infected with HIV or HCV is paramount[65].

The introduction of HAART has meant that HCV infection is now considered the principal cause of morbidity and mortality among HIV‑infected indi­viduals[10,49,66,67]. Liver-related morbidity occurs due to the acceleration of HCV-related disease, drug-induced hepatotoxicity, and, possibly, direct damage caused by HIV itself. Chronic viral hepatitis accounts for > 80% of liver-related deaths. End-stage liver disease and HCC are common complications in HIV-infected patients. Co-infection may accelerate clinical progression in both of these diseases, which are caused by HCV and HIV, and successful treatment for one disease is undermined if the other is neglected[45]. The infectious diseases physicians that care for HIV-infected patients with advanced HCV-related liver disease need to know how to assess a patient for advanced fibrosis, when to refer a patient for endoscopic screening for varices, and when/how to enroll patients in an HCC screening program[67]. Data from The TREAT Asia HIV Observational Database (TAHOD), a multi-center cohort of HIV patients in the Asia–Pacific region, showed that the impact of hepatitis co-infection on immunological and virological responses to ART, and on AIDS progression, are similar among Asian and Western populations[68]. That said, the high prevalence of HIV/HCV co-infection in Asian countries underscores the need to implement improved prevention and control measures because, compared with Western nations, fewer evidence-based prevention strategies are available.

***Medical management***

Hepatitis C has a limited impact on HIV disease progression. However, HIV does affect HCV with regard to several important areas[69]. The hepatitis C treatment goal is to eradicate HCV infection. Only then can complications associated with HCV-related liver disease, including HCC, be prevented. The therapy endpoint is the achievement of sustained virological response (SVR), defined as undetectable HCV RNA levels in the serum 24 wk after the completion of antiviral therapy. SVR is associated with an improved outcome in terms of liver fibrosis and reduced liver-related morbidity and mortality[59]. Similar results have been described in HIV/HCV co-infected patients[59].

The availability of Direct Acting Antivirals (DAAs) for the treatment of patients infected with HCV genotype 1 has markedly improved SVR[70]. The Asian Pacific Association for the Study of the Liver (APASL)[69] and other studies[49,71] suggest that DAAs, either with or without pegIFN + RBV, show much higher HCV eradication rates in HCV/HIV co-infected individuals than conventional pegIFN + RBV, with manageable toxicity and pharmacologic interactions. However, the promise of new oral DAAs comes with a substantial up-front financial cost, particularly for poorer Asian countries. Indeed, the majority of HCV-infected patients in low- or middle-income countries remain untreated. The global rollout of ART for HIV shows us that it is possible to make these agents both widely available and affordable[72]. Robust efforts to ensure equitable access to these advanced drugs for co-infected patients are imperative.

In the past, HIV-individuals were not considered candidates for solid organ transplantation due to concerns about a heightened risk of opportunistic infection and malignancy.However, recent single- and multi-center studies show that liver transplantation can be performed in HIV-infected patients who satisfy commonly accepted eligibility criteria, including an undetectable HIV RNA load in the plasma, current treatment with a stable HAART regimen or the ability to tolerate ART after transplantation, a minimum CD4+ T-cell count of 100–200 cells/mm3, and an absence of opportunistic infections[66].

**HBV/HCV/HIV TRIPLE INFECTION IN ASIA**

Few reports are available regarding the prevalence of HIV/HBV/HCV triple infection in Asia. The prevalence of triple infection in Chinese IDUs (19.1%) is a little bit higher than that in Burmese IDUs (10.4%) in the China-Myanmar border region, which is an important transfer station for drug trafficking from the “Golden Triangle”[53]. As we have seen in mainland Myanmar, triple infection is markedly low (0.35%)[19]. The other studies in mainland China show triple infection were 3.3% in a cohort study, that was carried out between 2010-2012[73] and 12.2% in central China[30]. Therefore, the endemicity of triple infection greatly varies even within the (China) country. Triple infection was not detected in North India[74], but it was manifested in 2.5% of subjects in South India[56], and in 4.8% in Indonesia[24].

HBV/HCV/HIV triple infection raised the chance of death, virological failure, and dropping out of care programs[73]. The incidence of hepatic decompensation was higher in patients with triple infection than in those with HIV/HCV co-infection[75].

**CONCLUSION**

Both HIV/HBV and HIV/HCV co-infection are highly prevalent in Asia. IDU, MSM, and geographic area are strong predictors for HBV, HCV, and HIV serostatus. Differences in the HBV and HCV co-infection rates among Asian countries may be due to the epidemiology of these viruses in specific countries/areas. Differences in the HBV/HIV co-infection rates. among countries are more pronounced than the differences in the HCV/HIV co-infection rates. The success of HBV vaccination programs and the HBV endemicity in a particular country may also play a role. Unlike HBV infection, the prevalence of which has been reduced by vaccination, HCV (which is mostly transmitted through the blood) cannot be tackled effectively in developing countries unless people are educated about the transmission routes and the dangers of certain practices. A detailed analysis of the progression and activity of liver disease in HIV co-infected patients is needed, along with the urgent implementation of comprehensive prevention strategies, such as community education and control programs, for both HBV/HIV and HIV/HCV co-infected individuals.

**REFERENCES**

1 **HIV/AIDS Programme.** Guidance on prevention of viral hepatitis B and C among people WHO inject drugs. WHO, 2012. Available from: URL: http: //apps.who.int/iris/bitstream/10665/75357/1/9789241504041\_eng.pdf

2 **Matthews PC**, Geretti AM, Goulder PJ, Klenerman P. Epidemiology and impact of HIV coinfection with hepatitis B and hepatitis C viruses in Sub-Saharan Africa. *J Clin Virol* 2014; **61**: 20-33 [PMID: 24973812 DOI: 10.1016/j.jcv.2014.05.018]

3 **Hoffmann CJ**, Thio CL. Clinical implications of HIV and hepatitis B co-infection in Asia and Africa. *Lancet Infect Dis* 2007; **7**: 402-409 [PMID: 17521593]

4 **Alter MJ**. Epidemiology of viral hepatitis and HIV co-infection. *J Hepatol* 2006; **44**: S6-S9 [PMID: 16352363]

5 **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**: 122-127 [PMID: 21459717]

6 **Utsumi T**, Yano Y, Lusida MI, Nasronudin M, Juniastuti H, Hayashi Y. Detection of highly prevalent hepatitis B virus co-infection with HIV in Indonesia. *Hepatol Res* 2013; **43**: 1032-1039 [PMID: 23336705 DOI: 10.1111/hepr.12053]

7 **Utsumi T**, Yano Y, Hotta H. Molecular epidemiology of hepatitis B virus in Asia. *World J Med Genet* 2014; **4:** 19-26 [DOI: 10.5496/wjmg.v4.i2.19]

8 **HIV/AIDS in the South-East Asia Region.** Progress Report 2011. World Health Organization. Regional Office for South-East Asia, 2012. Available from: URL: www.searo.who.int/entity/hiv/documents/hiv-aids\_in\_south-east\_asia.pdf

9 Review of the health sector response to HIV and AIDS in Indonesia 2007: World Health Organization Regional Office for South-East Asia 2007;2. Available from: URL: www.ino.searo.who.int/LinkFiles/HIV-AIDS\_and\_sexually\_transmitted\_infections\_Publications\_REVIEW\_HIV\_AIDS\_Indonesia\_2007

10 **Juniastuti**, Utsumi T, Nasronudin, Alimsardjono L, Amin M, Adianti M, Yano Y, Soetjipto, Hayashi Y, Hotta H, Lusida MI. High rate of seronegative HCV infection in HIV-positive patients. *Biomed Rep* 2014; **2**: 79-84 [PMID: 24649073]

11 **Abbas Z**, Siddiqui AR. Management of hepatitis B in developing countries. *World J Hepatol* 2011; **3**: 292-299 [PMID: 22216369 DOI: 10.4254/wjh.v3.i12.292]

12 **Núñez M**, Soriano V. Management of patients co-infected with hepatitis B virus and HIV. *Lancet Infect Dis* 2005; **5**: 374-382 [PMID: 15919623]

13 **Lacombe K**, Bottero J, Lemoine M, Boyd A, Girard PM. HIV/hepatitis B virus co-infection: current challenges and new strategies. *J Antimicrob Chemother* 2010; **65**: 10-17 [PMID: 19900950 DOI: 10.1093/jac/dkp414]

14 **Mehta KD**, Antala S, Mistry M, Goswami Y. Seropositivity of hepatitis B, hepatitis C, syphilis, and HIV in antenatal women in India. *J Infect Dev Ctries* 2013; **7**: 832-837 [PMID: 24240041 DOI: 10.3855/jidc.2764]

15 **Orito E**, Ichida T, Sakugawa H, Sata M, Horiike N, Hino K, Okita K, Okanoue T, Iino S, Tanaka E, Suzuki K, Watanabe H, Hige S, Mizokami M. Geographic distribution of hepatitis B virus (HBV) genotype in patients with chronic HBV infection in Japan. *Hepatology* 2001; **34**: 590-594 [PMID: 11526547]

16 **Fujisaki S**, Yokomaku Y, Shiino T, Koibuchi T, Hattori J, Ibe S, Iwatani Y, Iwamoto A, Shirasaka T, Hamaguchi M, Sugiura W. Outbreak of infections by hepatitis B virus genotype A and transmission of genetic drug resistance in patients coinfected with HIV-1 in Japan. *J Clin Microbiol* 2011; **49**: 1017-1024 [PMID: 21248087 DOI: 10.1128/JCM.02149-10]

17 **Yanagimoto S**, Yotsuyanagi H, Kikuchi Y, Tsukada K, Kato M, Takamatsu J, Hige S, Chayama K, Moriya K, Koike K. Chronic hepatitis B in patients coinfected with human immunodeficiency virus in Japan: a retrospective multicenter analysis. *J Infect Chemother* 2012; **18**: 883-890 [PMID: 22760340 DOI: 10.1007/s10156-012-0433-4]

18 **Koike K**, Kikuchi Y, Kato M, Takamatsu J, Shintani Y, Tsutsumi T, Fujie H, Miyoshi H, Moriya K, Yotsuyanagi H. Prevalence of hepatitis B virus infection in Japanese patients with HIV. *Hepatol Res* 2008; **38**: 310-314 [PMID: 17877726]

19 **Zaw SK**, Tun ST, Thida A, Aung TK, Maung W, Shwe M, Aye MM, Clevenbergh P. Prevalence of hepatitis C and B virus among patients infected with HIV: a cross-sectional analysis of a large HIV care programme in Myanmar. *Trop Doct* 2013; **43**: 113-115 [PMID: 23800421 DOI: 10.1177/0049475513493416]

20 **Fibriani A**, Wisaksana R, Alisjahbana B, Indrati A, Schutten M, van Crevel R, van der Ven A, Boucher CA. Hepatitis B virus prevalence, risk factors and genotype distribution in HIV infected patients from West Java, Indonesia. *J Clin Virol* 2014; **59**: 235-241 [PMID: 24529845 DOI: 10.1016/j.jcv.2014.01.012]

21 **Peters PJ**, McNicholl JM, Raengsakulrach B, Wasinrapee P, Mueanpai F, Ratanasuwan W, Intalapaporn P, Drobeniuc J, Ramachandran S, Thai H, Xia GL, Kamili S, Khudyakov Y, Weidle PJ, Teo CG, McConnell MS. An evaluation of hepatitis B virus diagnostic methods and responses to antiretroviral therapy among HIV-infected women in Thailand. *J Int Assoc Provid AIDS Care* 2013; **12**: 349-353 [PMID: 23792710 DOI: 10.1177/2325957413488201]

22 **Dunford L**, Carr MJ, Dean J, Nguyen LT, Ta Thi TH, Nguyen BT, Connell J, Coughlan S, Nguyen HT, Hall WW, Thi LA. A multicentre molecular analysis of hepatitis B and blood-borne virus coinfections in Viet Nam. *PLoS One* 2012; **7**: e39027 [PMID: 22720022 DOI: 10.1371/journal.pone.0039027]

23 **Saha D**, Pal A, Biswas A, Panigrahi R, Sarkar N, Sarkar J, Pal M, Guha SK, Saha B, Chakrabarti S, Chakravarty R. Characterization of treatment-naive HIV/HBV co-infected patients attending ART clinic of a tertiary healthcare centre in eastern India. *PLoS One* 2013; **8**: e73613 [PMID: 24023688 DOI: 10.1371/journal.pone.0073613]

24 **Anggorowati N**, Yano Y, Heriyanto DS, Rinonce HT, Utsumi T, Mulya DP, Subronto YW, Hayashi Y. Clinical and virological characteristics of hepatitis B or C virus co-infection with HIV in Indonesian patients. *J Med Virol* 2012; **84**: 857-865 [PMID: 22499006 DOI: 10.1002/jmv.23293]

25 **Kotaki T**, Khairunisa SQ, Sukartiningrum SD, Arfijanto MV, Utsumi T, Normalina I, Handajani R, Widiyanti P, Rusli M, Rahayu RP, Lusida MI, Hayashi Y, Nasronudin M. High prevalence of HIV-1 CRF01\_AE viruses among female commercial sex workers residing in Surabaya, Indonesia. *PLoS One* 2013; **8**: e82645 [PMID: 24367533 DOI: 10.1371/journal.pone.0082645]

26 **Aurpibul L**, Lumbiganon P, Kolasaraksa P, Hansudewechakul R, Sa-Nguanmoo P, Taeprasert P, Bunupuradah T, Poovorawan Y, Sirisanthana V, Puthanakit T. HIV and Hepatitis B coinfection among perinatally HIV-infected Thai adolescents. *Pediatr Infect Dis J* 2012; **31**: 943-947 [PMID: 22592516]

27 **He N**, Chen L, Lin HJ, Zhang M, Wei J, Yang JH, Gabrio J, Rui BL, Zhang ZF, Fu ZH, Ding YY, Zhao GM, Jiang QW, Detels R. Multiple viral coinfections among HIV/AIDS patients in China. *Biosci Trends* 2011; **5**: 1-9 [PMID: 21422594]

28 **Tsuchiya N**, Pathipvanich P, Rojanawiwat A, Wichukchinda N, Koga I, Koga M, Auwanit W, Kilgore PE, Ariyoshi K, Sawanpanyalert P. Chronic hepatitis B and C co-infection increased all-cause mortality in HAART-naive HIV patients in Northern Thailand. *Epidemiol Infect* 2013; **141**: 1840-1848 [PMID: 23114262 DOI: 10.1017/S0950268812002397]

29 **Zhou S**, Zhao Y, He Y, Li H, Bulterys M, Sun X, Dou Z, Robinson M, Zhang F. Hepatitis B and hepatitis C seroprevalence in children receiving antiretroviral therapy for human immunodeficiency virus-1 infection in China, 2005-2009. *J Acquir Immune Defic Syndr* 2010; **54**: 191-196 [PMID: 20032784 DOI: 10.1097/QAI.0b013e3181c99226]

30 **Chen X**, He JM, Ding LS, Zhang GQ, Zou XB, Zheng J. Prevalence of hepatitis B virus and hepatitis C virus in patients with human immunodeficiency virus infection in Central China. *Arch Virol* 2013; **158**: 1889-1894 [PMID: 23553454 DOI: 10.1007/s00705-013-1681-z]

31 **Gatanaga H**, Ibe S, Matsuda M, Yoshida S, Asagi T, Kondo M, Sadamasu K, Tsukada H, Masakane A, Mori H, Takata N, Minami R, Tateyama M, Koike T, Itoh T, Imai M, Nagashima M, Gejyo F, Ueda M, Hamaguchi M, Kojima Y, Shirasaka T, Kimura A, Yamamoto M, Fujita J, Oka S, Sugiura W. Drug-resistant HIV-1 prevalence in patients newly diagnosed with HIV/AIDS in Japan. *Antiviral Res* 2007; **75**: 75-82 [PMID: 17194486]

32 **Saravanan S**, Velu V, Kumarasamy N, Nandakumar S, Murugavel KG, Balakrishnan P, Suniti S, Thyagarajan SP. Coinfection of hepatitis B and hepatitis C virus in HIV-infected patients in south India. *World J Gastroenterol* 2007; **13**: 5015-5020 [PMID: 17854146]

33 **Saravanan S**, Madhavan V, Velu V, Murugavel KG, Waldrop G, Solomon SS, Balakrishnan P, Kumarasamy N, Smith DM, Mayer KH, Solomon S, Thyagarajan SP. High prevalence of hepatitis delta virus among patients with chronic hepatitis B virus infection and HIV-1 in an intermediate hepatitis B virus endemic region. *J Int Assoc Provid AIDS Care* 2014; **13**: 85-90 [PMID: 23722085 DOI: 10.1177/2325957413488166]

34 **Sulkowski MS**. Viral hepatitis and HIV coinfection. *J Hepatol* 2008; **48**: 353-367 [PMID: 18155314]

35 **Eun JR**, Lee HJ, Kim TN, Lee KS. Risk assessment for the development of hepatocellular carcinoma: according to on-treatment viral response during long-term lamivudine therapy in hepatitis B virus-related liver disease. *J Hepatol* 2010; **53**: 118-125 [PMID: 20471129 DOI: 10.1016/j.jhep.2010.02.026]

36 **Kurokawa M**, Hiramatsu N, Oze T, Yakushijin T, Miyazaki M, Hosui A, Miyagi T, Yoshida Y, Ishida H, Tatsumi T, Kiso S, Kanto T, Kasahara A, Iio S, Doi Y, Yamada A, Oshita M, Kaneko A, Mochizuki K, Hagiwara H, Mita E, Ito T, Inui Y, Katayama K, Yoshihara H, Imai Y, Hayashi E, Hayashi N, Takehara T. Long-term effect of lamivudine treatment on the incidence of hepatocellular carcinoma in patients with hepatitis B virus infection. *J Gastroenterol* 2012; **47**: 577-585 [PMID: 22231575 DOI: 10.1007/s00535-011-0522-7]

37 **Selabe SG**, Lukhwareni A, Song E, Leeuw YG, Burnett RJ, Mphahlele MJ. Mutations associated with lamivudine-resistance in therapy-naïve hepatitis B virus (HBV) infected patients with and without HIV co-infection: implications for antiretroviral therapy in HBV and HIV co-infected South African patients. *J Med Virol* 2007; **79**: 1650-1654 [PMID: 17854040]

38 **Sereno L**, Mesquita F, Kato M, Jacka D, Nguyen TT, Nguyen TN. Epidemiology, responses, and way forward: the silent epidemic of viral hepatitis and HIV coinfection in Vietnam. *J Int Assoc Physicians AIDS Care* (Chic) 2012; **11**: 311-320 [PMID: 22828983]

39 **Aizawa M**, Tsubota A, Fujise K, Kato T, Sakamoto M, Ohkusa T, Tajiri H. Highly active antiretroviral therapy improved persistent lamivudine-resistant viremia in acute hepatitis B virus genotype Ae infection with coinfection of human immunodeficiency virus. *Hepatol Res* 2010; **40**: 229-235 [PMID: 20377825 DOI: 10.1111/j.1872-034X.2009.00570.x]

40 **Maimaiti R**, Zhang Y, Pan K, Wubuli M, Andersson R. Frequent coinfection with hepatitis among HIV-positive patients in Urumqi, China. *J Int Assoc Provid AIDS Care* 2013; **12**: 58-61 [PMID: 23087203 DOI: 10.1177/1545109712446176]

41 **Reuter S**, Oette M, Wilhelm FC, Beggel B, Kaiser R, Balduin M, Schweitzer F, Verheyen J, Adams O, Lengauer T, Fätkenheuer G, Pfister H, Häussinger D. Prevalence and characteristics of hepatitis B and C virus infections in treatment-naïve HIV-infected patients. *Med Microbiol Immunol* 2011; **200**: 39-49 [PMID: 20853118 DOI: 10.1007/s00430-010-0172-z]

42 **Wisaksana R**, Indrati AK, Fibriani A, Rogayah E, Sudjana P, Djajakusumah TS, Sumantri R, Alisjahbana B, van der Ven A, van Crevel R. Response to first-line antiretroviral treatment among human immunodeficiency virus-infected patients with and without a history of injecting drug use in Indonesia. *Addiction* 2010; **105**: 1055-1061 [PMID: 20331555 DOI: 10.1111/j.1360-0443.2010.02898.x]

43 **Yang R**, Gui X, Xiong Y, Gao SC, Yan Y. Impact of hepatitis B virus infection on HIV response to antiretroviral therapy in a Chinese antiretroviral therapy center. *Int J Infect Dis* 2014; **28**: 29-34 [PMID: 25236390 DOI: 10.1016/j.ijid.2014.07.018]

44 **Ghate M**, Tripathy S, Gangakhedkar R, Thakar M, Bhattacharya J, Choudhury I, Risbud A, Bembalkar S, Kadam D, Rewari BB, Paranjape R. Use of first line antiretroviral therapy from a free ART programme clinic in Pune, India - a preliminary report. *Indian J Med Res* 2013; **137**: 942-949 [PMID: 23760381]

45 **Ye S**, Pang L, Wang X, Liu Z. Epidemiological implications of HIV-hepatitis C co-infection in South and Southeast Asia. *Curr HIV/AIDS Rep* 2014; **11**: 128-133 [PMID: 24682917]

46 **Rockstroh JK**, Bhagani S, Benhamou Y, Bruno R, Mauss S, Peters L, Puoti M, Soriano V, Tural C. European AIDS Clinical Society (EACS) guidelines for the clinical management and treatment of chronic hepatitis B and C coinfection in HIV-infected adults. *HIV Med* 2008; **9**: 82-88 [PMID: 18257771]

47 **Andreoni M**, Giacometti A, Maida I, Meraviglia P, Ripamonti D, Sarmati L. HIV-HCV co-infection: epidemiology, pathogenesis and therapeutic implications. *Eur Rev Med Pharmacol Sci* 2012; **16**: 1473-1483 [PMID: 23111959]

48 **Hagan H**, Neurer J, Jordan AE, Des Jarlais DC, Wu J, Dombrowski K, Khan B, Braithwaite RS, Kessler J. Hepatitis C virus infection among HIV-positive men who have sex with men: protocol for a systematic review and meta-analysis. *Syst Rev* 2014; **3**: 31 [PMID: 24669911]

49 **Sulkowski MS**. Current management of hepatitis C virus infection in patients with HIV co-infection. *J Infect Dis* 2013; **207** Suppl 1: S26-S32 [PMID: 23390302 DOI: 10.1093/infdis/jis764]

50 **Chang YJ,** Hsieh J, Peng CY, Li J, Hser YI. HIV and HCV Serostatus and Knowledge Among Patients in Urban Versus Rural Methadone Maintenance Clinics in Kunming. *J Drug Issues* 2014; **44:** 281 [DOI: 10.1177/0022042613511438]

51 **Beyrer C**, Razak MH, Lisam K, Chen J, Lui W, Yu XF. Overland heroin trafficking routes and HIV-1 spread in south and south-east Asia. *AIDS* 2000; **14**: 75-83 [PMID: 10714570]

52 **Jia M**, Luo H, Ma Y, Wang N, Smith K, Mei J, Lu R, Lu J, Fu L, Zhang Q, Wu Z, Lu L. The HIV epidemic in Yunnan Province, China, 1989-2007. *J Acquir Immune Defic Syndr* 2010; **53** Suppl 1: S34-S40 [PMID: 20104107]

53 **Zhou YH**, Liu FL, Yao ZH, Duo L, Li H, Sun Y, Zheng YT. Comparison of HIV-, HBV-, HCV- and co-infection prevalence between Chinese and Burmese intravenous drug users of the China-Myanmar border region. *PLoS One* 2011; **6**: e16349 [PMID: 21283696]

54 **Lu Y**, Robinson M, Zhang FJ. Human immunodeficiency virus and hepatitis C virus co-infection: epidemiology, natural history and the situation in China. *Chin Med J* (Engl) 2009; **122**: 93-97 [PMID: 19187624 DOI: 10.3760/cma.j.issn.0366-6999.2009.01.017]

55 **Chandra N**, Joshi N, Raju YS, Kumar A, Teja VD. Hepatitis B and/or C co-infection in HIV infected patients: a study in a tertiary care centre from South India. *Indian J Med Res* 2013; **138**: 950-954 [PMID: 24521641]

56 **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 [PMID: 22926367]

57 **Karki S**, Ghimire P, Tiwari BR, Shrestha AC, Gautam A, Rajkarnikar M. Seroprevalence of HIV and hepatitis C co-infection among blood donors in Kathmandu Valley, Nepal. *Southeast Asian J Trop Med Public Health* 2009; **40**: 66-70 [PMID: 19323036]

58 **Soriano V**, Martin-Carbonero L, Vispo E, Labarga P, Barreiro P. [Human immunodeficiency virus infection and viral hepatitis]. *Enferm Infecc Microbiol Clin* 2011; **29**: 691-701 [PMID: 21978797 DOI: 10.1016/j.eimc.2011.07.003]

59 **Fernández-Montero JV**, Soriano V. Management of hepatitis C in HIV and/or HBV co-infected patients. *Best Pract Res Clin Gastroenterol* 2012; **26**: 517-530 [PMID: 23199509]

60 **Graham CS**, Baden LR, Yu E, Mrus JM, Carnie J, Heeren T, Koziel MJ. Influence of human immunodeficiency virus infection on the course of hepatitis C virus infection: a meta-analysis. *Clin Infect Dis* 2001; **33**: 562-569 [PMID: 11462196]

61 **Soriano V**, Vispo E, Labarga P, Medrano J, Barreiro P. Viral hepatitis and HIV co-infection. *Antiviral Res* 2010; **85**: 303-315 [PMID: 19887087]

62 **Busch MP**, Kleinman SH, Nemo GJ. Current and emerging infectious risks of blood transfusions. *JAMA* 2003; **289**: 959-962 [PMID: 12597733]

63 **Wasley A**, Alter MJ. Epidemiology of hepatitis C: geographic differences and temporal trends. *Semin Liver Dis* 2000; **20**: 1-16 [PMID: 10895428]

64 **Alter MJ**. Prevention of spread of hepatitis C. *Hepatology* 2002; **36**: S93-S98 [PMID: 12407581]

65 **Mateu-Gelabert P**, Gwadz MV, Guarino H, Sandoval M, Cleland CM, Jordan A, Hagan H, Lune H, Friedman SR. The staying safe intervention: training people who inject drugs in strategies to avoid injection-related HCV and HIV infection. *AIDS Educ Prev* 2014; **26**: 144-157 [PMID: 24694328 DOI: 10.1521/aeap.2014.26.2.144]

66 **Camino N**, Sheldon J, Soriano V. Update on hepatitis C treatment in HIV-coinfected patients. *Minerva Gastroenterol Dietol* 2004; **50**: 67-77 [PMID: 15719008]

67 **Curry MP**. HIV and hepatitis C virus: special concerns for patients with cirrhosis. *J Infect Dis* 2013; **207** Suppl 1: S40-S44 [PMID: 23390304 DOI: 10.1093/infdis/jis763]

68 **Zhou J**, Dore GJ, Zhang F, Lim PL, Chen YM. Hepatitis B and C virus coinfection in The TREAT Asia HIV Observational Database. *J Gastroenterol Hepatol* 2007; **22**: 1510-1518 [PMID: 17645479 DOI: 10.1111/j.1440-1746.2007.05062.x]

69 **Omata M,** Kanda T, Yu M, Yokosuka O, Lim S, Jafri W, Tateishi R, Hamid SS, Chuang W, Chutaputti A, Wei L, Sollano J, Sarin SK, Kao J, McCaughan GW. APASL consensus statements and management algorithms for hepatitis C virus infection. *Hepatol Int* 2012; **6**: 409–435 [DOI: 10.1007/s12072-012-9342-y]

70 **Rockstroh JK**, Bhagani S. Managing HIV/hepatitis C co-infection in the era of direct acting antivirals. *BMC Med* 2013; **11**: 234 [PMID: 24228933]

71 **Kabiri M**, Jazwinski AB, Roberts MS, Schaefer AJ, Chhatwal J. The changing burden of hepatitis C virus infection in the United States: model-based predictions. *Ann Intern Med* 2014; **161**: 170-180 [PMID: 25089861 DOI: 10.7326/M14-0095]

72 **Jayasekera CR**, Barry M, Roberts LR, Nguyen MH. Treating hepatitis C in lower-income countries. *N Engl J Med* 2014; **370**: 1869-1871 [PMID: 24720680]

73 **Zhang F**, Zhu H, Wu Y, Dou Z, Zhang Y, Kleinman N, Bulterys M, Wu Z, Ma Y, Zhao D, Liu X, Fang H, Liu J, Cai WP, Shang H. HIV, hepatitis B virus, and hepatitis C virus co-infection in patients in the China National Free Antiretroviral Treatment Program, 2010-12: a retrospective observational cohort study. *Lancet Infect Dis* 2014; **14**: 1065-1072 [PMID: 25303841 DOI: 10.1016/S1473-3099(14)70946-6]

74 **Gupta S**, Singh S. Hepatitis B and C virus co-infections in human immunodeficiency virus positive North Indian patients. *World J Gastroenterol* 2006; **12**: 6879-6883 [PMID: 17106941]

75 **Lo Re V**, Wang L, Devine S, Baser O, Olufade T. Hepatic decompensation in patients with HIV/Hepatitis B Virus (HBV)/Hepatitis C Virus (HCV) triple infection versus HIV/HCV coinfection and the effect of anti-HBV nucleos(t)ide therapy. *Clin Infect Dis* 2014; **59**: 1027-1031 [PMID: 24944235 DOI: 10.1093/cid/ciu476]

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**Table 1 Prevalence, risk factors, and the main vital genotypes identified in hepatitis B virus/human immunodeficiency virus co-infected individuals in Asia**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Country** | **Prevalence (%)** | **Risk factors** | **Main genotype** | **Ref.** |
| Southeast Asia |  |  | | |
| Indonesia | 3.2  15.3  7.0 | Sexual  IDU  Men with IDU | B3  B3  B3, D1, B2, C1 | Anggorowati *et al*[24], 2012  Utsumi *et al*[6], 2013  Fibriani *et al*[20], 2014 |
| Myanmar | 8.7 | Homosexual men |  | Zaw SK *et al*, 2013[19] |
| Thailand | 13.0  3.3  11.9 | HB vaccination Women |  | Aurpibul *et al*[26], 2012  Peters *et al*[21], 2013  Tsuchiya *et al*[28], 2013 |
| Vietnam | 28.0  15.2  10.3 | IDU  CSW | B4,B2,C1,  C5 | Dunford *et al*[22], 2012  Sereno *et al*[38], 2012 |
| East Asia |  |  | | |
| China | 4.9  6.3  7.2  6.1 | Older children Ethnicity  Sexual  Sexual |  | Zhou *et al*[29]*,* 2010  He *et a l* [27], 2011  Maimaiti[40], 2012  Chen *et al*[30], 2013 |
| Japan | 8.8  6.4  7.9  6.0 | Homosexual men  Homosexual men  Homosexual men  Homosexual men | Ae | [Gatanaga](http://www.ncbi.nlm.nih.gov/pubmed?term=Gatanaga%20H%5BAuthor%5D&cauthor=true&cauthor_uid=17194486) *et al*[31], 2007  Koike *et al*[18], 2008  Fujisaki *et al*[16], 2011  Yanagimoto *et al*[17], 2012 |
| South Asia |  |  | | |
| India | 9.0  11.3  1.5 | Hetero Sexual  Hetero Sexual Men | D > A > C | [Saravanan](http://www.ncbi.nlm.nih.gov/pubmed?term=Saravanan%20S%5BAuthor%5D&cauthor=true&cauthor_uid=17854146) *et al*[32], 2007  Saha *et al*[23], 2013  Saravanan *et al*[33], 2014 |

IDU: Injecting drug user; CSW: Commercial sex worker.**Table 2 Antiretroviral therapies for hepatitis B virus/human immunodeficiency virus co-infection, and drug-resistant mutations in Asian countries**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | **Indonesia** | **Japan** | **Thailand** | **Vietnam** | **China** | **India** |
| Recommendation for ART on HBV/HIV Co-infection | Initiate with WHO clinical stage IV and/or a CD4 count less than 200/mm3[42] | TDF + 3TC/FTC-based regimen | Screening for HBV.  Two antiretroviral regimen with anti-HBV/anti-HIV activity (*e.g.*, TDF, 3TC) | TDF-based regimen | Combination of TDF with FTC or 3TC | HBeAg positivity is indicator to initiate ART with combination of two dually-active drugs |
| Currently used therapy for HBV/HIV Co-infection | Telbivudine (LdT)  Lamivudine (3TC)  Zidovudine (ZDV)  Nevirapine (NVP)  Efavirenz (EFV)  Stavudine (d4T)  Tenofovir (TDF) | 3TC  Entecavir (ETV)  TDF  Adefovir dipivoxil (ADV)  Emtricitabine (FTC) | 3TC  Nevirapine (NVP)  EFV  Stavudine (d4T) | Stavudine (d4T) 3TC  NVP | d4T  ZDV  3TC  NVP  EFV[43] | ZDV  3TC  NVP  EFV  d4T  [44] |
| Drug-resistant mutation | Lamivudine  M204I  M204I+L180M | Lamivudine1  *V173L + L180M + M204V*  Lamivudine  L180M, M204V, L217R  M184V, I195M | Lamivudine  M204V/I | Lamivudine  L180M  M204V |  | Lamivudine1  *M204V*  *L180M* |

1Lamibudin naïve case. WHO: World Health Organization; HBV: Hepatitis B virus; HIV: Human immunodeficiency virus.