Hot News

Coinfection with Viral Hepatitis in HIV patients in 2023

According to UNAIDS roughly 1.5 million new HIV infections occur each year worldwide. The number of persons living with HIV (PLWH) is estimated around 38 million globally, of whom 25 million live in Sub-Saharan Africa. Despite increasing rates of antiretroviral treatment uptake, approximately 15% of infected carriers are still not treated. This is mostly due to difficulties in access to medical care (mostly in Third World regions) or because infected persons are not aware of their status (and are neither tested nor diagnosed). As consequence, this subset of infected persons does not benefit from antiretrovirals individually (and, therefore, may progress to AIDS) and is the major source for HIV transmission to others, since treated individuals having undetectable viral load are not infectious, a phenomenon known as U=U (undetectable=untransmittable) (*De Cock et al. Emerg Infect Dis 2021*).

Since immunodeficiency directly caused by HIV is largely halted thanks to the wide use of antiretroviral therapy, comorbidities have become an important cause of clinical complications and shorter survival in PLWH. Given shared transmission routes, nowadays, chronic viral hepatitis is among the most frequent causes of morbidity in PLWH. This is particularly true in Sub-Saharan Africa, where high prevalence rates occur, along with lower access to antiviral therapies *(Kenfack-Momo et al. PLoS One 2022).*

Hepatitis viruses B, C, and delta may cause chronic liver disease and are the major cause of hepatocellular carcinoma (HCC) worldwide. Given shared transmission routes, during the past decades, however, effective antivirals have been developed to treat hepatitis B and C. For hepatitis B, oral antiviral therapy with tenofovir suppresses viremia in most treated patients, although HBV is not eradicated. Hence, treatment needs to be given lifelong. The rate of HBV-related hepatic decompensation events has declined, although HCC still may develop due to a direct oncogenic effect of HBV (*Ramos-Rincon et al. Aliment Pharmacol 2023*).

Coinfection	Estimated population (million)
HIV and HBV	2.7
HIV and HCV	1.5
HIV and HDV	0.5
HIV, HBV and HCV	0.3
HIV, HCV and HDV	0.2

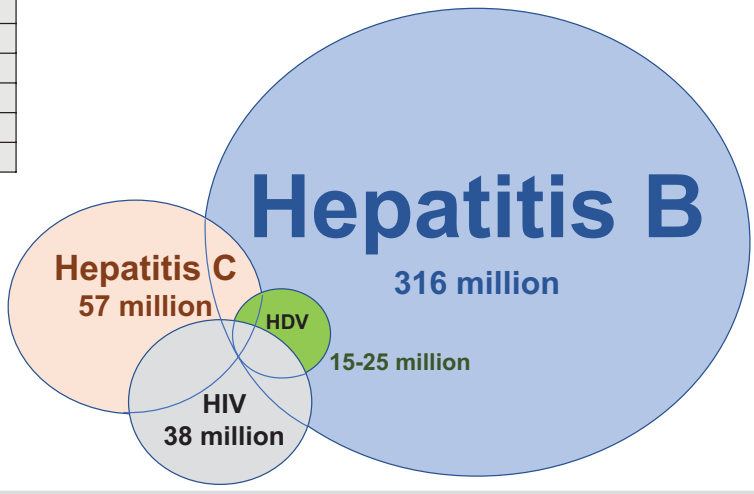

Figure 1. *Global estimates of PLWH and chronic viral hepatitis.*

For hepatitis C, the introduction of direct-acting antivirals has transformed the prognosis of infected persons with significant reductions in complications both hepatic and extra-hepatic (*Ramos-Rincon et al. Hepatol Int 2022; Ogawa et al. JAMA Intern Med 2023*). Indeed, 2-3 months of oral HCV antiviral therapy allows to eradicate (cure) the infection in most treated patients.

The introduction of antivirals for hepatitis B and C has changed the landscape of HIV coinfections in Western countries. Indeed, decompensation events in cirrhotics and HCC have become less frequent in PLWH, as it has been noticed in the general population. Figure 1 shows the current estimates of PLWH with distinct viral hepatitis (*Platt et al. Lancet Infect Dis 2016; Beguelin et al. Liver Int 2023*). For hepatitis C, nearly one million coinfected persons have been treated since 2015, although HCV reinfections have mitigated cure rates.

The current figures do not record temporal trends. The big picture shows that the slowdown in numbers and clinical burden of viral hepatitis among PLWH seems to have reached a plateau. There are three major reasons for this finding, one for each of the hepatitis viruses. First, HBV antivirals can control but not cure hepatitis B. The virus stays in the liver of HBsAg+ patients and may prone to liver cancer even in the absence of cirrhosis.

Second, given that there is no protective immunity, HCV re-infections are frequent in persons that continue to be engaged in high-risk behaviors, either sexual promiscuity mostly among men having sex with men or needle sharing among persons who inject drugs. In these two groups, new exposures to HCV may blunt the benefit of any prior curative course of HCV therapy.

Third, the lack of effective therapy for hepatitis delta explains that chronic HDV infection is taking over hepatitis B or C as cause of morbidity and mortality in PLWH. Chronic HDV infection occurs in roughly 15% of PLWH and hepatitis B (*Soriano et al. AIDS 2011; Beguelin et al. Liver Int 2023*). As hepatitis delta is the most aggressive of all chronic viral hepatitis, most PLWH with hepatitis delta progresses to liver cirrhosis and may develop liver cancer (*Fernandez-Montero* et al. *Clin Infect Dis 2014; Beguelin et al. 2017*). No effective antiviral therapy has been developed to date as cure of hepatitis delta, although a subcutaneous entry inhibitor, bulevirtide, has recently been approved (*Soriano et al. Drug Des Devel Ther 2023*).

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Received in original form: 04-01-2023
Accepted in final form: 11-02-2023
DOI: 10.24875/AIDSRev.M23000060