

The burden of HIV-1 and HIV-2 epidemics in Ivory Coast

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Abstract

Simian immunodeficiency viruses (SIV) infecting chimpanzees (SIV_{cpz}) and sooty mangabeys (SIV_{sm}) are, respectively, the biological precursors of human immunodeficiency viruses (HIV) Types 1 and 2. Former French colonies in West Africa are the regions where retroviruses first jumped from primates to humans. Ivory Coast is nowadays a country of over 29 million people, being 2% (580,000) persons living with HIV (PLWH). However, one-quarter remains undiagnosed. Heterosexual transmission is by far the most frequent mechanism of HIV acquisition and women exhibit higher rates of infection than men. Despite preventive measures, HIV infection in children throughout breastfeeding remains significant. The proportion of PLWH carrying HIV-1 is rising whereas conversely HIV-2 carriers are steadily declining. A nationwide survey conducted on earlier 2024 showed that a total of 188,880 PLWH were on follow-up. HIV-1 infection was found in 163,947, HIV-2 in 5,114, and coinfection in 3,182. HIV type was not reported for 7,500. Antiretroviral therapy with tenofovir, lamivudine, and dolutegravir is by far the most frequently prescribed regimen in Ivory Coast (n = 168,543). Viral suppression is recognized in 94.3% of treated PLWH, despite one-third acknowledging unwanted treatment interruptions after failure of stock supplies. Given shared transmission routes with HIV, coinfection with other human retroviruses such as Human T-lymphotropic virus type-1 (HTLV-1) and/or hepatitis viruses B, C, and delta are frequent in Ivory Coast. Coinfections remain largely undiagnosed and poorly managed. In summary, the HIV pandemic caused by both HIV-1 and HIV-2 is a major public health challenge in Ivory Coast, where strategies for expanding diagnosis, sustain antiretroviral treatment, and manage coinfections warrant further efforts.

Keywords

HIV-1. HIV-2. Antiretroviral therapy. Drug resistance. Pregnant women. Hepatitis B. Hepatitis C. HTLV-1. Dolutegravir.

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Introduction

The HIV/AIDS pandemic is disproportionately affecting the African continent. Of the estimated 39 million people living with HIV (PLWH) globally, over 26 million live in Africa. Many of the former French colonies in West Africa exhibit some of the largest HIV infection rates.

Ivory Coast has an extension of 300,000 km² and over 29 million population (Fig. 1). It is a poor country, ranking 170 out of 186 listed by the United Nations. Recent estimates show that 2% (580,000) of the population is HIV positive. However, 25% remain undiagnosed. Whereas the proportion infected with HIV-1 has been rising, HIV-2 carriers are steadily declining. In a nationwide survey conducted on earlier 2024, only 188,880 PLWH were on follow-up. HIV-1 was found in 163,947, HIV-2 in 5,114, and coinfection in 3,182. HIV type was not reported for 7,500.

Both HIV-1 and HIV-2 are believed to represent inter-species transmissions from simian immunodeficiency viruses (SIV) infecting primates and monkeys to humans in West Africa. Zoonotic jumps occurred during the last century, being HIV-1 transmitted from chimps in Cameroon around 1900¹ and HIV-2 from sooty mangabeys in Ivory Coast around 1960². Interestingly, SIVs infecting their respective animal reservoirs replicate actively but do not cause disease^{3,4}, whereas the same viruses may lead to AIDS when infect humans.

The current major transmission routes for HIV-1 and HIV-2 in Ivory Coast are sexual and vertical. It should be highlighted that roughly 60% of the population in Ivory Coast is < 25 years old. New HIV infections are frequently seen in teenage girls acquired from older men, as reported in other Sub-Saharan countries^{5,6}. The yearly birth rate is of 34/1000, one of the greatest worldwide. Children born and breastfed from women unaware of their HIV infection or not treated are a major source of pediatric infections.

Antiretroviral treatment

The combination of tenofovir, lamivudine, and dolutegravir (TLD) is by far the most frequently prescribed antiretroviral regimen in low and middle-income countries, including Ivory Coast. TLD has several advantages over other antiretroviral regimens⁷, including low risk for selection of drug resistance, good antiviral activity on HIV-2, cross-activity on Hepatitis B virus (HBV), few drug interactions allowing first-line treatment of tuberculosis and other opportunistic infections, etc.

In a recent nationwide survey, viral suppression was 94.3% in 168,543 PLWH treated with antiretrovirals in Ivory Coast, despite unwanted treatment interruptions after failing stock supplies were acknowledged by one-third of patients. Breaking of stock supplies was much more frequent during the COVID-19 pandemic⁸, but thereafter access to medications has steadily returned to normality.

The vast majority of patients treated with tenofovir in Ivory Coast receive the old formulation of tenofovir disoproxil fumarate, which can lead to nephrotoxicity in a subset of treated patients. Given that kidney disease and renal insufficiency are more frequent in the black ethnicity⁹, the use of the new tenofovir alafenamide formulation, which is less nephrotoxic, should be pushed in African countries.

The advent of long-acting antiretroviral medications is appealing for a large subset of HIV patients that challenge with daily oral therapies. Poor drug adherence is associated with treatment failure and selection of drug resistance. However, TLD-sparing tenofovir, such as the commonly recommended combination of injectable cabotegravir and rilpivirine, depicts several limitations, including lower activity against HIV-2, more frequent selection of drug resistance, more drug interactions, and a lack of efficacy on Hepatitis B¹⁰.

Experience at Centre Médico-Social Walé

This is a large outclinic located in Yamoussoukro, the country's capital town. The city has roughly 400,000 population. The HIV program is run with the support of PEPFAR since year 2006. A total of 1349 PLWH were on regular follow-up until June 2024. Only 10 of them were infected with HIV-2, being two women coinfecting with HIV-1. All HIV-2 patients but two were female.

Antiretroviral treatment prescribed was TLD for 1280. Only 5.1% were taken other medications, including abacavir (n = 48), zidovudine (n = 14), and/or efavirenz (n = 7).

The rate of PLWH on regular follow-up is steadily on the rise (Fig. 2). Women aged between 25 and 49 years old are by far the largest group, whereas men predominate in the group aged over 50 years old (Fig. 3).

HIV-2

Around half of the sooty mangabeys living in the Tai forest, located in the southwestern part of Ivory Coast,

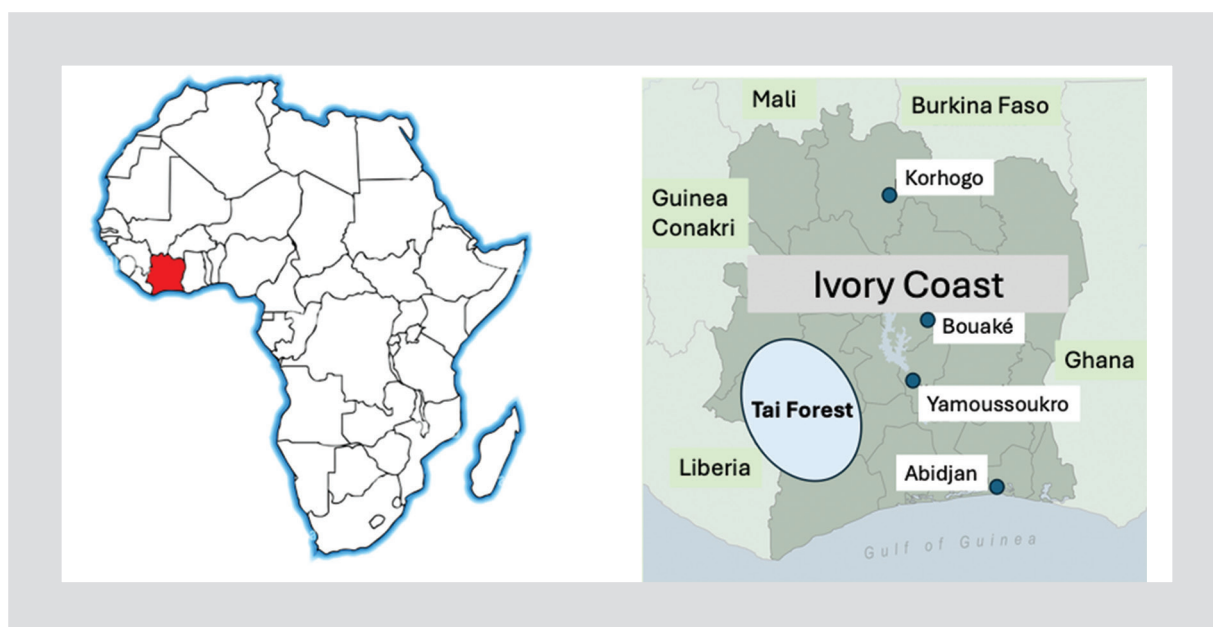


Figure 1. Ivory Coast geographical location, largest cities, and the Tai forest.

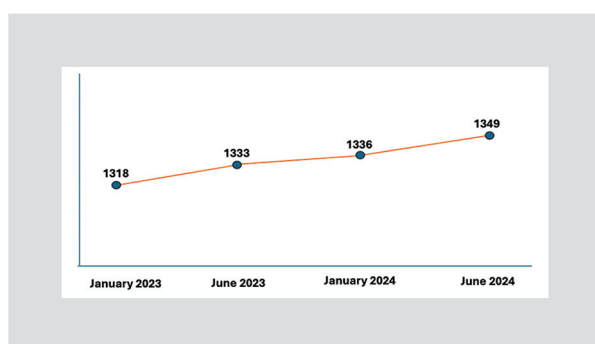


Figure 2. Persons living with HIV on regular follow-up at the Centre Médico-Social Walé.

are infected with SIV². The first cases of HIV-2 in humans were reported in the mid-1980s, including migrants from Ivory Coast living in France¹¹. Molecular and serological surveys conducted at that time suggested a high rate of PLWH and a relatively high proportion of HIV-2 in the country^{12,13}. However, as in other countries in West Africa and globally, since the 2000s HIV-2 cases have been going down whereas HIV-1 has risen taken over¹⁴.

HIV-2 differs from HIV-1 being less pathogenic and transmissible, and showing a distinct sensitivity to anti-retroviral agents. Typically, there is a lack of efficacy of non-nucleoside reverse transcriptase inhibitors (i.e., efavirenz, nevirapine, rilpivirine, or doravirine) on

HIV-2¹⁰. This is an important reason to distinguish at diagnosis HIV-1 from HIV-2 in HIV-seropositive individuals. Otherwise, mistakes managing these patients may occur¹⁵.

Coinfection with other viruses causing chronic illnesses

HIV-1 and HIV-2 share mechanisms of transmission with other viruses that establish chronic infections, such as human T-lymphotropic virus type-1 (HTLV-1), another human retrovirus, and Hepatitis B, C, and delta viruses. Therefore, individuals at increased risk for HIV-1 and HIV-2 are more frequently coinfecting with one or several of these other viruses¹⁶. However, the likelihood of contagion by either sexual, parenteral, or perinatal exposure differs for each of these agents (Table 1).

The advent of point-of-care tests to be used at least once in PLWH would facilitate the recognition of coinfections in low-income countries, such as Ivory Coast. These rapid tests are already available for HBsAg, anti-hepatitis C virus (HCV), anti-HIV-2, and anti-HTLV-1¹⁷⁻¹⁹.

HTLV-1

The rate of simian T-lymphotropic virus 1 (STLV-1) infection among non-human primates has been reported

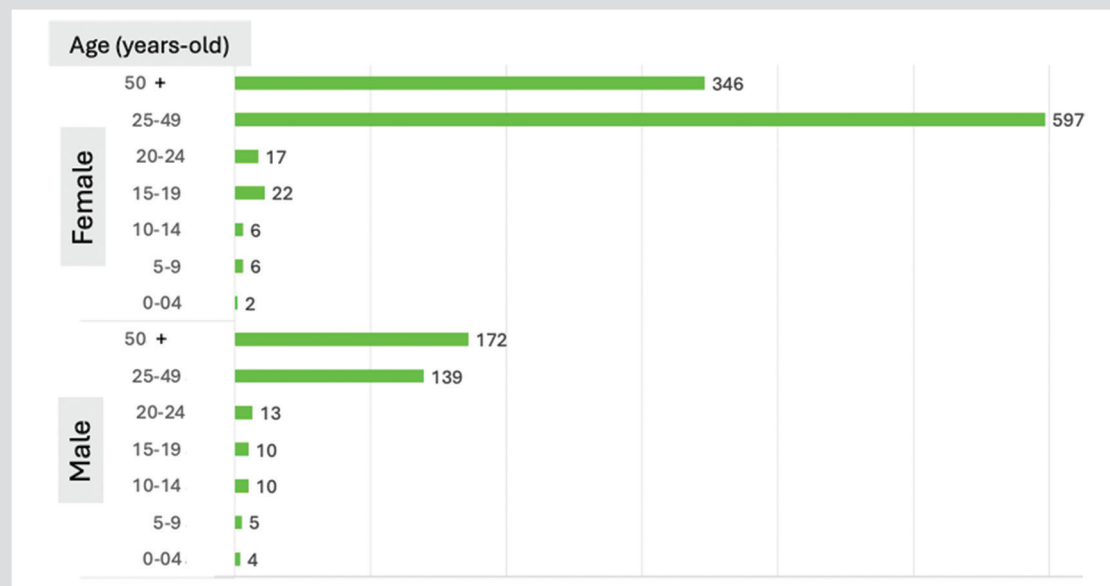


Figure 3. Persons living with HIV on regular clinical follow-up by sex and age.

Table 1. Main human bloodborne chronic viral infections

| Virus | Main clinical manifestations | Transmission route | | |
|-----------------|---|--------------------|------------|-----------|
| | | Sexual | Parenteral | Perinatal |
| HIV-1 | AIDS | ++ | +++ | ++ |
| HIV-2 | | + | ++ | + |
| HTLV-1 | TSP/HAM ATL | + | ++ | + |
| Hepatitis B | Liver cirrhosis Hepatocellular carcinoma | +++ | +++ | +++ |
| Hepatitis C | | + | +++ | + |
| Hepatitis delta | | ++ | +++ | ++ |

TSP/HAM: tropical spastic paraparesis/HTLV-associated myelopathy; ATL: adult T-cell leukemia.

to be as high as 50% among sooty mangabeys, chimps, and red colobus at the Tai forest in Ivory Coast. Human hunting activities and bushmeat provide multiple opportunities for continuous zoonotic infections²⁰⁻²². Among humans, HTLV-1 is mostly transmitted throughout sexual contact, blood transfusions, and breastfeeding. Although many infected carriers remain asymptomatic lifelong, around 10% develop life-threatening illnesses, such as subacute myelopathies and T-cell lymphomas, for which treatment options are poor²³.

Between 10 and 15 million people worldwide are infected with HTLV-1. There are hot spots of infection in Japan, the Caribbean basin, South America, Australia, Iran, and Romania²⁴. Reliable information on HTLV rates in Sub-Saharan Africa is scarce²⁵. However, given the proximity with animal reservoir habitats, HTLV-1 infection rates in West Africa must be high. The introduction of rapid tests (point-of care) for screening HTLV antibodies¹⁹ would provide a nice opportunity for collecting this information and plan

prevention programs, as it is already being pursued in Europe²⁶.

Hepatitis B

Chronic HBV infection is recognized by the presence of persistent serum HBsAg in persons exposed to the virus at least 6 months earlier. Chronic Hepatitis B is the most frequent cause of liver cirrhosis and hepatocellular carcinoma worldwide²⁷. Liver cancer is particularly frequent in Africa²⁸.

Over 250 million people are estimated to suffer from chronic Hepatitis B globally. Given that most carriers are asymptomatic, only 10% are diagnosed. The rest are unaware of their infection and do not benefit from any monitoring and/or treatment. Furthermore, preventive interventions cannot be taken for contacts, including newborns of infected mothers²⁹.

One study conducted in the year 2022 reported a 7.7% prevalence rate of chronic Hepatitis B in Ivory Coast, which represents 2.1 million people. However, only 33,000 (2%) had been diagnosed. Furthermore, of 500,000 patients estimated to be eligible for HBV treatment, only 1,200 were on antiviral therapy³⁰.

With respect to children < 5 years old, the estimated prevalence in Ivory Coast was 0.8%, which represents 40,000 children with chronic Hepatitis B. Protection with HBV vaccination had been given to 91% of children < 1 year of age but birth doses only to 66%²⁹. In children and adolescents up to 16 years old, the prevalence of chronic Hepatitis B increases up to 5%. HIV coinfection, maternal HBsAg positivity, lack of HBV vaccination, and scarifications are associated with this higher rate^{29,31}.

The HIV and Hepatitis B epidemics are interconnected with shared routes of transmission and specific antiviral drugs that are effective against both viruses. Nearly, 300 million people around the world live with chronic Hepatitis B, many of whom are from risk populations who could benefit from HIV prevention services³¹. Oral pre-exposure prophylaxis (PrEP) for HIV with tenofovir has implications in the prevention and treatment of HBV infection, but many people at increased risk of HIV acquisition may instead prefer long-acting formulations of PrEP (i.e., with injectable cabotegravir or implantable rings with doravirine), which are currently not active against HBV³².

Ideally, PrEP programs would offer both oral and long-acting formulations of antiretrovirals along with HBV screening to optimize HIV prevention services and HBV prevention and care. People who are not immune to HBV would benefit from being vaccinated

against HBV before initiating long-acting PrEP³². People who remain non-immune to HBV despite vaccination may benefit from being offered oral, tenofovir-based PrEP given its potential for HBV PrEP. People using PrEP and living with HBV who are not linked to dedicated HBV care would also benefit from laboratory monitoring at PrEP sites to ensure safety when using and after stopping tenofovir. PrEP programs are ideal venues to offer HBV screening, HBV vaccination for people who are non-immune, and treatment with tenofovir-based PrEP for people with indications for HBV therapy³².

Hepatitis C

The HCV is an RNA flavivirus that produces chronic infection in roughly two-thirds of individuals exposed. The virus is mostly transmitted by parenteral contact, following blood transfusions, injections using non-sterilized needles, etc. However, contagions both perinatally and through sexual contact may occur. Men having sex with men are particularly prone to experience both acute and chronic Hepatitis C³³.

The global prevalence of chronic Hepatitis C was estimated around 65 million one decade ago. Then, oral direct-acting antivirals (DAA) were developed and begun been used widely in developed regions and a few low-middle-income countries. As a result, a significant decline in the number of chronic Hepatitis C carriers has occurred. New estimates were of 57 million HCV carriers by 2020³⁴. However, access to DAA is quite limited outside rich countries and both HCV diagnosis and treatment are rather than suboptimal in most Sub-Saharan countries, including Ivory Coast³⁵. Thus, the prevalence of Hepatitis C in Ivory Coast has kept high and unchanged during the last decade³⁶.

Given the efficacy and safety of sofosbuvir, along with its high resistance profile and pangenotypic activity, oral sofosbuvir-based combinations given for 3 months are being pursued as HCV treatment for low and middle-income countries³⁷.

Hepatitis delta

The hepatitis delta virus (HDV) is a small RNA satellite virus that only produces human infection when associated to HBV. However, chronic hepatitis delta is the most severe form of viral liver disease, leading faster to cirrhosis and hepatocellular carcinoma than chronic Hepatitis B or C³⁸. As Hepatitis B, most cases

of HDV transmission occur following sexual and parenteral exposures.

In one study conducted 10 years ago in Ivory Coast, the rate of anti-delta antibodies among HBsAg+ was 15%³⁹. However, the clinical impact of hepatitis delta in the country, especially among the HIV-coinfected population, is unknown.

Conclusion

The HIV pandemic caused by both HIV-1 and HIV-2 is a major public health challenge in Ivory Coast, where strategies for expanding diagnosis and sustain antiretroviral treatment warrant major efforts. Furthermore, given shared transmission routes, PLWH exhibit a high rate of coinfection with other retroviruses such as HTLV-1, and bloodborne hepatitis viruses B, C, and delta. There is an urgent need for universal screening of these infections in PLWH and provide proper management to coinfecting individuals in Ivory Coast.

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Conflicts of interest

None.

Ethical considerations

Protection of humans and animals. The authors declare that no experiments involving humans or animals were conducted for this research.

Confidentiality, informed consent, and ethical approval. The authors have obtained approval from the Ethics Committee for the analysis of routinely obtained and anonymized clinical data, so informed consent was not necessary. Relevant guidelines were followed.

Declaration on the use of artificial intelligence. The authors declare that no generative artificial intelligence was used in the writing of this manuscript.

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