Research Article

HIV-2 Incidence Decline in West Africa - A Perspective on the Need for Vigilance

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Abstract | In the context of the epidemiology of HIV/AIDS in West Africa, the declining incidence of HIV-2 elicits mixed feelings of victory and doubt. Previously, we published a systematic literature review which identified factors contributing to this declining trend but also raised concerns about its sustainability. The aim of this article is to caution against interpreting this trend as a triumph against HIV/AIDS in the region. This caution is deserved due to serious challenges in West Africa that require liberal attention. These include; inadequate diagnostic methods and algorithms for monitoring HIV-2, the possibility of dangerous genetic mutations and resurgence of super-strains, cross-reactivity of HIV types that interfere with accurate reporting of HIV-2 cases, and suboptimal/neglected treatment and care (S/NTC) for HIV-2 individuals. Additionally, gaps in surveillance infrastructure, health inequality in classifying HIV burdens based on HIV type, and deprived HIV-2 research and policy enforcement could create obscurity in HIV-2 data. Considering the existing circumstances, this article highlights the importance of vigilance, re-evaluation of assumptions, and advocacy for unified efforts to address the multidimensional problems associated with HIV-2 to guarantee the sustained integrity of public health.

Introduction

There are two different trends of HIV epidemiology in West Africa: The decline in the incidence of HIV-2 and the persistence of HIV-1. The former appears to offer a sense of victory in the broader campaign against HIV/AIDS but also raises doubts about the true nature of the situation, given the factors protesting the incidence of the disease and the lack of congregated epidemiologic data (Lauya *et al.*, 2023; UNAIDS, 2023). We suspect that the viral strain may be undergoing deceptive reinforcement and could bounce back, especially that there are reported subtypes (Chen *et al.*, 1997; Damond *et al.*, 2004; Smith *et al.*, 2008), and changes in natural phenomena that would make the virus unlikely to be eradicated (Woolhouse *et al.*, 2012; Diamandis, 2022). Previously, we raised further concerns about

the decline in HIV-2 cases, questioning "whether the factors responsible are sufficient to keep the virus in its nature and maintain the current pattern of the disease in West Africa" (Lauya et al., 2023). Regardless of the case, there is a need for careful thought to interpret the status and implications of HIV-2 not only for immediate necessity but also for preparedness against impending viral resurgence. This is a strong possibility because of the ever-adapting nature of HIV, which is characterized by a high rate of genetic mutation, suggesting that we cannot afford to uphold complacency. Besides, there are cautious suggestions as that from Diamandis who re-emphasized the importance of implementing lessons learned from the COVID-19 pandemic to prevent unintended microbial threats. He considered the human-virus relationship "The mother of all battles" (Diamandis, 2022).

If we put the HIV strains side by side, there is a clear indication that HIV-2 has been under the umbrella of HIV-1 both in terms of research and resource allocation. The perceived low pathogenicity of HIV-2 (Gottlieb et al., 2018) and supposedly, health system adaptation hastened this triviality. However, in the new world, plagued with unpredictable microbial evolution and changes in natural phenomena, there should be no justification valid enough to rule out the possibility of potential dangers associated with HIV-2. Misunderstanding the epidemiological status of the disease holds the risk of spreading the virus beyond regional borders, weakening our collective efforts against HIV/AIDS and hindering equitable access to health and well-being.

The declining incidence of HIV-2 seems to create an illusory sense of security, tempting us to overlook latent vulnerabilities, especially for economically broke populations, where the spotlight on HIV-1 might unintentionally ignore HIV-2. Thus, we proclaim a hidden threat and advocate for skepticism toward the declining statistics. We must continue to be vigilant, understanding the complex nature of the virus and acting with far sightedness and resilience before the door to address this embryonic challenge closes.

Challenges and implications of the decline in HIV-2 incidence in West Africa

HIV diagnostic algorithm: The accurate diagnosis of HIV-2 infection is the backbone for achieving broader epidemiological and patient management goals (Berry, 2013). However, there is a large gap between these needs and access to suitable diagnostic systems in West Africa, especially due to deficient diagnostic algorithms, inefficient RDTs, and gaps in resistance testing.

The current diagnostic algorithm designed for HIV-1 falls short in classifying HIV-2 due to inherent genetic and antigenic differences (Shah et al., 2022). Likewise, the ability of the serologic enzyme-linked immunosorbent assay (ELISA) to accurately classify HIV types is suboptimal (Yuksel et al., 2018). Moreover, rapid diagnostic tests (RDTs) for HIV diagnosis have serious limitations; RDTs exhibit inaccuracies, low sensitivity and specificity, high rates of false HIV diagnoses, and cross-reactivity issues (Ceccarelli et al., 2021). The management of HIV-2 in West Africa is further limited by the difficulty of quantifying the HIV-2 RNA load in the laboratory, as well as scarcity of commercial laboratories equipped for this task (Berry, 2013; Shah et al., 2022; Damond et al., 2008; Vallefuoco et al., 2016). Consequently, our ability to monitor HIV-2 at the species level is lacking. Additionally, the unavailability of HIV-2 phenotypic and genotypic resistance testing, along with a lack of clear guidance in interpreting mutations, complicates diagnostic insufficiencies (Shah et al., 2022). Meanwhile, it is possible to use the Cobas HIV-1/HIV-2 qualitative assay to discriminate between HIV types (Duncan et al., 2021), but the method is rarely available.

This multifaceted situation has contributed to the decline in the incidence of HIV-2 in West Africa. This means that most patients go unnoticed, leading to increased morbidity and mortality and underestimation of cases. The absence of a clear HIV-2 testing algorithm allows the virus to not only remain undiagnosed and undetected within marginalized populations but also opens the door for the resurgence of super-pathogenic and treatment-resistant strains. These gaps in diagnostics challenge our ability to obtain trustworthy data, and will delay our efforts to quickly identify and control potentially dangerous HIV-2 evolution. See the HIV testing algorithm here (Shah et al., 2022).

Chance of genetic mutation and recombination

The dynamic genetic recombination and rapid mutation rates of retroviruses are fertile ground for the evolution of novel HIV strains, which are ever-

present and evolving threats (Vignuzzi *et al.*, 2006; Pond *et al.*, 2012; Pérez-Losada *et al.*, 2015). Nearly every known genome of HIV viruses globally has developed mechanisms that outrun our defences, and various variants have become resistant to all available antiviral drugs (WHO, 2021). The diversity and re-emergence of HIV genes suggest that it is reasonable to expect the classification of potential variants of HIV-2 (Woolhouse *et al.*, 2012). Furthermore, consistent with the typical characteristics of RNA viruses, HIV-2 has higher mutation rates than its host cells, sometimes reaching a million times greater (Duffy, 2018). Generally, viral mutations are catastrophic and fuel the virus's adaptation and resistance. However, as Duffy noted, such mutations can also rarely backfire, during which the virus mutants generate self-damaging errors (Duffy, 2018). Moreover, the current state of fragile health infrastructure in West African settings introduces the possibility of delays in identifying a more pathogenic form of the HIV-2 strain (Azevedo, 2017; Adebisi *et al.*, 2021). If more dangerous subtypes of HIV-2 emerge, there is a risk that significant harm may occur before identifying and controlling them. Woolhouse and colleagues strongly advised adopting an effective global surveillance system for novel viruses (Woolhouse *et al.*, 2012).

HIV cross-reactivity

Patients infected with HIV-1 often generate an immune response that similarly cross-reacts to HIV-2 during coinfection due to antigenic similarities (Karlsson *et al.*, 2019). This phenomenon is not limited to natural immune responses but extends to diagnostic testing procedures. The commonly used diagnostic methods available in West Africa, such as enzyme immunoassays (EIAs) and rapid diagnostic tests (RDTs), are limited by these concepts, thus impacting diagnostic accuracy and patient management (Gottlieb *et al.*, 2018; Hønge *et al.*, 2018). Cross-reactivity between HIV strains poses a risk of diagnostic confusion, hindering the accurate determination of the true incidence of each strain in the population. Consequently, the reported decrease in HIV-2 incidence may not reflect the actual situation, potentially masking the ongoing presence and spread of HIV-2. This raises concerns about the effectiveness of current diagnostic algorithms in accurately monitoring the decline of the disease in the region. Undetected, misclassified, or overlooked HIV-2 cases present a latent threat to public health.

Although advanced polymerase chain reaction (PCR) methods, such as the Cobas HIV-1/HIV-2 qualitative assay are available for differentiating between HIV and other pathogens (Vallefuoco *et al.*, 2016; Duncan *et al.*, 2021; Tchounga *et al.*, 2023), these tools face the reality of limited accessibility and affordability in West Africa. As a result, the use of serologic tests such as RDTs persists. This reliance on serologic tests with potential cross-reactivity offers the disadvantage of misdiagnosis and false classification of HIV, consequentially leading to poor patient management and lack of accurate data.

Suboptimal/neglected treatment and care (S/NTC)

Despite the challenges and ambiguity surrounding HIV-2 statistics, 1.2 million people in West Africa are estimated to be infected with the virus, the highest not observed anywhere (Lauya *et al.*, 2023; Gottlieb *et al.*, 2018; Mendoza *et al.*, 2020). Regardless of the lower global profile of HIV-2 patients than HIV-1 patients, these individuals do not deserve reluctance in treatment and care. Unfortunately, the reality in West Africa is no other than this.

Suboptimal/neglected treatment and care (S/NTC) for HIV-2 patients increases the chance of morbidity, which can lead to slower but progressive transmission dynamics within the population. Similarly, S/NTC encourages disease progression, leading to increased mortality rates due to AIDS (Lauya *et al.*, 2023; Ceccarelli *et al.*, 2021). Furthermore, when treatments are suboptimal or neglected, the viability of the virus is enhanced, leading to treatment failure and drug resistance. This is the case because the current treatment for HIV-2 follows the treatment algorithms for HIV-1, which are associated with massive drug resistance problems (Shah *et al.*, 2022; Ceccarelli *et al.*, 2021). Accordingly, the true impact of S/NTC is two edged: Firstly, it is suggestive of a cause of declining incidence of HIV-2 as we previously reported (Lauya *et al.*, 2023). Secondly, it is a key determinant of the progressive and prolonged burden of the disease in West Africa.

Surveillance challenges

The health surveillance systems in West Africa do not match the disease burden in the region. Most revealing is that no West African country surpasses the minimal cut-off of 15% for achieving universal health coverage (Adebisi *et al.*, 2021). The top three are Ghana (8.43%), Cape Verde (8.29%), and Burkina

Faso (7.60%) (Adebisi *et al.*, 2021). There are various limitations, including insufficient laboratories and infrastructure, supposed lack of skilled human resources, ethical issues, and potentially overwhelming growth in human population size (Adebisi *et al.*, 2021; Aborode *et al.*, 2021; Bassey and Miteu, 2023). However, unique surveillance challenges exist for HIV-2 patients due to its lower global profile compared to that of HIV-1 patients.

In many countries in West Africa, there is a concerning lack of data on the incidence of HIV-1/HIV-2 (Lauya *et al.*, 2023; Joshi *et al.*, 2021). The limited availability and accessibility of diagnostic tests specifically designed to detect and differentiate between HIV-1 and HIV-2 can be attributed to this lack of data (Damond *et al.*, 2008). These deficiencies increase the possibility of misdiagnosing and underreporting HIV-2 infections. Consequently, our understanding of the true extent of the virus has been limited. Another challenge is the limited awareness and knowledge about HIV among health workers (Umeh *et al.*, 2008), as well as the asymptomatic nature of HIV-2 infection and its slower pathogenic processes. This situation creates the risk of missed opportunities for proper testing and treatment for individuals infected with HIV-2.

Surveillance and testing programs for HIV-2 is deprived. This is justified by the obvious continued focus on HIV-1. Without effective surveillance, it is difficult to gather useful data for implementing effective public health policies. Prioritizing HIV-1 without considering HIV-2 is akin to fighting HIV with only half the information, because the rapid molecular and genetic evolutions of the virus could create unique differences between the two strains. This preference may lead to uninformed policies and strategies that would undermine the overall HIV response. It increases the risk of underestimating the number of HIV-2 cases, ultimately resulting in new cases in other parts of the world, as already observed in Europe, India, and the United States (Campbell-Yesufu and Gandhi, 2011; Saraiya *et al.*, 2018).

Global health inequalities
According to the Joint United Nations Programme on HIV/AIDS (UNAIDS), inequalities, including gender-based issues, stigmatization, discrimination, discrepancies in resource allocation, and neglected children's access to healthcare, are key indicators of

progressive HIV/AIDS cases (UNAIDS, 2022). To mitigate these international and local issues, the World Health Organization (WHO) launched the Health Inequality Data Repository in April 2023. This repository prioritized current health and development issues, including HIV (Kirkby *et al.*, 2023; Hosseinpoor *et al.*, 2023). While this is good news, it is important to consider inequalities in terms of specific viral strains of morbidities. For example, let us recognize the ingenuity of HIV data in West Africa, given that two different strains of the virus (HIV-1 and HIV-2) are implicated in the disease. Preference for one strain over the other not only nurtures potential disasters but also sets aside vulnerable populations, such as sex workers and homosexuals (Djomand *et al.*, 2014; Stannah *et al.*, 2023). This inequality further hinders their access to healthcare services, including HIV testing and treatment. Consequently, neglecting HIV-2 in West Africa will contribute to global health inequalities. Considering the interconnectedness of our world, HIV-2 will continue to spread sporadically until it reaches an alarming threshold, undermining the United Nations (UN) efforts toward global health equity. If we fail to address the partiality of classifying HIV burden based on specific viral strains, the HIV/AIDS we are up against may only be partially threatened.

Conclusions and Recommendations

The following limits HIV-2 management in West Africa: inadequate diagnostic systems, including ineffective testing algorithms, unreliable rapid diagnostic tests, unavailable resistance tests, and the issue of cross-reactivity between HIV-1 and HIV-2 during testing. There is also inequality in classifying HIV burdens based on HIV type and designing specific policies. Furthermore, healthcare providers often overlook HIV-2 patients, resulting in suboptimal treatment and care. All of these factors raise doubts about the reliability of the reported decline in HIV-2 incidence in the region. We caution that the supposedly declining statistics on HIV-2 could be premature victory against HIV/AIDS. We emphasize the need for improved diagnostic systems and processes, strengthened surveillance systems, optimized treatment and care, and addressed inequality in HIV-2 management. By strengthening these areas, we can ensure more equitable patient management and obtain reliable HIV-2 data, which will in turn sustain progress in the ongoing battle

against HIV/AIDS in West Africa. Where the HIV-2 incidence is declining as the case may be, the virus is not disappearing. We suggest that there should be no place for health system adaptation where either strain of HIV is marginalized or prioritized; the fight against HIV/AIDS should remain robust and all inclusive.

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Novelty Statement

This article provides novel perspective on the declining incidence of HIV-2 in West Africa. While this trend is celebrated, the authors argue that this perception overlook critical issues. Our opinion can lead to more nuanced understanding of the HIV-2 situation in West Africa and direct better strategies for managing the virus.

Author's Contribution

LL conceptualized and wrote the manuscript.
PNO, NTC and ICC contributed to the writing of the manuscript.
All the authors read and approved the final manuscript.

Conflict of interest
The authors have declared no conflict of interest.

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