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Review Article

Molecular Epidemiology Of Hiv-1 In African Countries: A Comprehensive Overview.

Marta Giovanemtti, Massimo Ciccozzr, Cristinrt Parolin and Alessandpha Borsetti.

University of Health Sciences, Ankara Bilkent City Hospital.

Abstract

Since it first appeared in non-human primates in West-central Africa, the human immunodeficiency virus type 1 (HIV-1) has killed about 33 million people worldwide, making it a serious public health concern. Over 20 million people in Africa are thought to be living with HIV/AIDS and that over 730,000 new HIV-1 infections still happen year, most likely as a result of limited testing access.A single infected patient may develop many viral variations in a single day due to the great genetic heterogeneity of HIV-1, which is caused by a rapid replication cycle and high mutation rate. Consequently, the ongoing observation and description of
A major obstacle to more targeted diagnoses, treatments, care, and intervention efforts is the presence of HIV-1 subtypes and recombinant forms in African nations. To demonstrate the seriousness of the HIV-1 danger among African nations and to gain a better understanding of virus genetic diversity and dispersion dynamics, a succinct description of all the subtypes and recombinant forms circulating in Africa is provided in this paper.

Keywords: *HIV-1; Africa; subtypes; circulating recombinant form (CRF); recombinant.*

INTRODUCTION

One of the biggest threats to global public health is the Human Immunodeficiency Virus type 1 (HIV-1) [1,2]. The HIV-1 epidemic grew quickly around the world, aided by stigma, prejudice, and pervasive inequality that are today a significant obstacle to AIDS (acquired immunodeficiency disease) resolution [1–3]. It is gaining ground in nations where AIDS is already the major cause of death and swiftly spreading into regions that were comparatively immune to the epidemic [1,2]. The Joint United Nations Program on HIV/AIDS (UNAIDS) projects that 38 million persons worldwide will be HIV/AIDS positive by the end of 2020.Even though there has been a 23% decrease in new HIV-1 infections since 2010, Sub-Saharan Africa is still the most afflicted region, home to an estimated 69% of all HIV AIDS patients, and the epidemic is still fueled by gender-based violence and inequality [1, 2, 4–6]. In African countries, 25.7 million people with HIV-1, which also makes up about two-thirds of all new HIV-1 infections worldwide. In Africa, there were almost 1.5 million new HIV-1 infections in 2020 [1,2]. States in northern and southern Africa have very different AIDS epidemics.Because people in Northern Africa tend to follow fewer high-risk cultural practices that encourage the spread of viruses, their prevalence rates are much lower [1, 2, 7, 8]. About 25% of new infections occur in Southern Africa, making it the most affected region on the continent. Heterosexual relationships are the primary means of transmission in Africa, and sexual violence and sex work play a major role in the disease's spread [1,9]. In terms of genetic diversity, HIV-1 is most prevalent in Africa. The purpose of this review is to provide an overview of the prevalence of HIV-1 subtypes and recombinant forms in nations in Africa.

HIV ORIGIN

Through a process called zoonosis, HIV-1 first infected non-human primates in West-central Africa before spreading to humans in the early 20th century [10–12]. According to retrospective research, HIV-1 originated in the Democratic Republic of the Congo and then spread to other regions in West Africa and sub-Saharan Africa [12–14]. Cross-species

***Corresponding Author:** Marta Giovanemtti, University of Health Sciences, Ankara Bilkent City Hospital.
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transmissions of the simian immunodeficiency virus from non-human primates to humans also resulted in the introduction of the Human Immunodeficiency Virus type 2 (HIV-2) [14,15]. Although its frequency is declining, HIV-2 is primarily found in West Africa, where an estimated 1-2 million people are infected [16].Compared to HIV-1, HIV-2 is less harmful and development to immunodeficiency happens more slowly [16]. There are nine different subtypes of HIV-2 (A-I), with group A being the most common and group B coming in second. and CRF01_AB, a single circulating recombinant form (CRF) [15,16].

HIV-1 GENETIC DIVERSITY

Throughout its global spread, HIV-1 underwent significant molecular diversification [17–20]. About one mutation per genome is produced by each HIV-1 replication cycle.

Four reasons are primarily responsible for this exceptional rate of viral mutation: (i) The reverse activity the high rate of viral replication; (ii) the tendency of HIV-1 to undergo genetic recombination during replication; (iv) host selective immune pressures; and (iii) transcriptase, which promotes the accumulation of transcription errors that the enzyme is unable to correct because it lacks 30 to 5′ exonuclease activity [19–23]. As a result, the viral population may rapidly experience significant genetic divergence, giving rise to closely related but unique viral variations.

This variability includes intrahost variability (6–19%) that occurs within the same individual as well as interhost variability (2–5%) that occurs between the viral populations infecting different individuals [23–25]. The range of variance among subtypes is based on the genomic areas and subtypes analyzed, ranging from 20 to 35%. Although it can reach up to 30%, inter-subtype sequence diversity is typically between 8 and 17% [23–25]. Recombinant viruses may arise via concurrent (co-infection) or sequential (super-infection) infection by distinct HIV-1 strains, significantly enhancing HIV-1 genetic diversity [26–28].

HIV-1 SUBTYPES AND RECOMBINANTS

Four phylogenetic HIV-1 groups may be distinguished using full viral genome sequencing, mostly by characterizing the env and/or gag genomic regions: M (major), O (outlier), N (non-M/non-O), and the most recent group P [29, 30]. Group M viruses, in contrast, have The other groups N, O, and P have not been extensively distributed and barely account for ~1% to 2% of all HIV-1 infections, despite having dominated the global HIV-1 pandemic since its beginning [29–31]. Group M comprises about 95% of all isolated strains and can be further divided into two F (F1–F2) sub-subtype areas (Figure 1), six A (A1–A6), and nine subtypes (A–D, F–H, J, K) [29–33].Three different HIV-1 strains have been identified in the Democratic Republic of the Congo, resulting in the formation of a new, unique subtype known as subtype L [34, 35]. Depending on the subtypes and genomic regions, genetic variation within subtypes can range from 8 to 20%, whereas variance between subtypes typically varies from 17 to 35%. investigated [19,24,26]. Discrete and randomly distributed breakpoints across genomic regions in recombinant viruses can be found using phylogenetic analysis [19,24,26]. The so-called “mosaic” strains of HIV-1, known as circulating recombinant forms (CRF) [19,24,26,29], are the result of genetic recombination and are characterized by full-length or nearly full-length HIV-1 sequences present in at least three epidemiologically unrelated individuals [24,29]. CRFs are rather prevalent; as of November 2020, the Los Alamos National Laboratory had registered 106 CRFs.The recombinant subtypes that make up the genomic structure and the order in which they are reported determine the names of the CRFs. CRF01_AE and CRF02_AG are the most common CRFs in the global HIV-1 pandemic. CRF01_AE, a recombinant of a subtype, was the first CRF to be discovered. containing subtypes A gag, pol, and E vif, vpr, env, nef, and long terminal repeat (LTR), as well as a probable extinct subtype E ancestor. With subtypes A gag, env, subtype A/G pol, tat, rev, nef, and subtype G LTR, CRF02_AG is a recombinant of subtypes A and G [36–38]. CRFs with three or more distinct HIV-1 strains are known as “complex” recombination of several subtypes [24, 29].The diverse category known as unique recombinant forms (URFs) is made up of a variety of subtypes that exhibit distinct recombination breakpoints. They were taken from a single multiply infected person only once, in contrast to the CRFs [19,24,29,39]. An elevated A percentage of URFs from West and Central African nations as well as the Republic of the Congo has already been reported [40]. In Eastern Africa, where subtypes A, C, and D are most common, the AD and AC inter-subtype recombinants have been discovered [30]. In certain instances, the accurate classification of virus genome sequences falls outside the known diversity, and not all HIV-1 lineages have been thoroughly described.As a result, “U” stands for untyped for these sequences [19,26]. Since new viral sequences are constantly being discovered and the classification of various HIV-1 subtypes is prone to change, classifying HIV-1 strains continues to be a challenging task [41]. The most recent estimate of HIV-1 Subtype C accounts for 46.6% of infections globally in 2010–15, followed by subtype B (12.1%), subtype A (10.3%), subtype G (4.6%), subtype D (2.7%), F, H, J, and K combined (0.9%), CRF02_AG (7.7%), CRF01_AE (5.3%), other CRFs (3.7%), and URFs (6.1%) [29–33,41].The world’s most common subtypes are CRF01_AE in Asia, CRF02_AG in Western and Central Africa, subtype B in the Americas, Europe, and Oceania, subtype C in Southern Africa and India, and subtype A in the Soviet Union and portions of East Africa [42, 43]. The HIV-1 gene’s genetic variations can impact the

virus's mechanism of transmission and interaction with the target cell, the infection's clinical course, and the response to treatment, as evidenced by variations in transmission rates and disease progression among subtypes [42–47]. Although subtype C is the most common worldwide, it is unknown if there are phenotypic variations from the other subtypes that allow for its increased pathogenicity or transmission efficiency [44,45].CRF01_AE and subtype D have been linked to accelerated disease progression. The survival rates of the D and A subtypes differed significantly, according to an analysis of a sizable cohort in Uganda [48]. According to a comprehensive survey conducted in China, subjects

Compared to those with a non-CRF01_AE subtype, those with the CRF01_AE subtype showed a quicker loss of CD4+T cells and HIV/AIDS progression [49]. The existing evidence for survival is insufficient to make firm conclusions, and a number of factors, such as host genetic and immunologic responses, may influence the disparities in disease progression rates among subtypesHuman migration, conflict, mobility, geographic isolation, and cultural factors all play a part in the complicated and dynamic process of HIV-1 subtype and recombinant form geographic distribution and diffusion in African locations. as well as sexual aspects [49–54]. The growing genetic variety of HIV-1 has important ramifications for drug resistance testing, vaccine development, and viral pathogenicity, all of which depend on current understanding of the geographic distribution of HIV-1 subtypes and recombinant forms.

Distribution of Subtypes and Recombinants in African Regions

By examining a total of 204,573 HIV-1 samples, each with a minimum length of 500 bp, gathered between 1990 and 2020, and accessible through a public database (Los Alamos: https://www.hiv.lanl.gov/content/index), the HIV-1 distribution over the African continent over time was ascertained. African nations were grouped into five major regions: Northern, Western, Eastern, Central, and Southern, as defined by the UNAIDS classification, with some adjustments made to account for the social, cultural, and religious aspects as well as the geopolitical aspects of the regions.While Central nations have a history of armed conflict, a significant number of refugee-related issues, and food shortages, Northern countries share similar cultural norms [55]. Eastern and Western nations are grouped together. according to where they are located. The Southern region's countries have the highest HIV-1 prevalence in the world, with 20% of adults living with the virus.

According to a cumulative analysis of HIV-1 distribution in Africa (204,573 samples) covering the years 1990–2020, or the whole pandemic period, subtype B has predominated in Northern Africa (53.04%). Most commonly, the CRF02_AG has been found in Western and Central Africa.

(53.66% and 26.61%, respectively), but subtype C has been the most prevalent overall in Eastern and Southern Africa (44.15 and 98.44%, respectively).

Calculating the macroregional distribution of CRFs, URFs, and HIV-1 subtypes throughout the most recent five-year period, 2015–2020,The two maps differ noticeably from one another. Northern Africa is dominated by subtype B HIV-1, with a discernible increase in CRF02_AG. CRF02_AG and subtype G are more prevalent in Western and Central Africa, despite the presence of multiple CRFs and URFs as well as all important subtypes. represented as well. A sizable portion of URFs and subtypes D, C, and A primarily affect Eastern Africa. Subtype C is almost entirely responsible for the outbreak in Southern Africa.

To examine changes in the prevalence of all HIV-1 subtypes, CRFs, and UFRs in African regions from 1990 to 2020—and most recently in the last five years—the data was split into four time periods: 1990–1999, 2000–2009, 2010–2014, and 2015–2020.Overall, between 2000 and 2009, the percentage of cumulative occurrence of subtypes, recombinants, and untyped forms grew; nevertheless, subtype F, group N, and CRF06_cpx and CRF22_01_A1 expanded between 2010 and 2020, and group O made a significant

contribution from 1990 to 1999. The rise in subtypes G and J as well as the recombinants CRF02_AG, CRF09_cpx, CRF22_01_A1, and URFs are the primary characteristics of the last five years, from 2015 to 2020.Specifically, the dataset was divided into four time periods: 1990–1999, 2000–2009, 2010–2020, and 2015–2020 in order to assess the relative contributions of each subtype and recombinant form across time. Most of the HIV-1 that has been circulating in Africa since the start of the epidemic is

category C, which accounted for almost half (42.4%) of all infections between 2000 and 2009, was followed by proportionate variations of subtypes A, D, G, and CRF02_AG in declining order. URFs contribute significantly in all time periods. Over the past five years, there has been a decline in subtype C (30.48) and an increase in recombinants, CRF02_AG (10.63), and URFs (30).

SUMMARY

Despite a lengthy history of HIV-1 transmission, African nations still face challenges in effectively managing the virus and responding to public health emergencies. Actively tracking and characterizing HIV-1 genetic variability across the African continent is a significant issue that will allow for more precise diagnosis, care, therapy, and intervention techniques. Distinct geographic zones with varying distributions of HIV-1 subtypes and recombinant forms are shown by an analysis of HIV-1 distribution throughout Africa during the course of the epidemic's thirty years. Subtype B generally affects

the Northern region, subtype C mostly affects the Southern region, CFR02_AG primarily affects the Western and Central regions, and subtype C dominates the Eastern region.

A thorough analysis of the distribution of HIV-1 subtypes and recombinants within the most recent time frame (2015–2020) shows that there is significant subtype diversity and dynamic changes in certain areas.

For instance, subtype B used to prevail in Northern Africa, but within the past five years,A significant rise in certain recombinant forms, such as CRF02_AG and other CRFs, indicates that CRFs are spreading across this epidemic. Since 1990, subtype C has been the most common in Southern Africa. However, a more thorough examination of this time frame revealed that subtype C was somewhat declining in 2010–2020, even if there has been a significant decline in the previous five years. There are millions of HIV-1-positive individuals in this region, and a number of factors may have helped to slow the spread and diversification of subtype C. For instance, the quick expansion of antiretroviral medication has resulted in a 30% decrease in HIV-1-related mortality from 2010 to 2017 (UNAIDS, 2020).In the macroregions where several subtypes co-circulate, these three recombinants are contributing more to the AIDS epidemic. The notable rise in CRFs and the shifting trends in the regional distribution of recombinant forms and HIV-1 subtypes demonstrates the need for molecular surveillance over time. HIV-1 variability's practical implications include how it affects the effectiveness of novel medications and therapeutic approaches. It's possible that more resistant strains will spread, particularly in nations with little resources.Given that HIV-1 genotypes affect drug resistance and susceptibility [56], surveillance is necessary to guarantee proper diagnosis, treatment plans, and outcomes, especially for the less prevalent subtypes, CRFs, and URFs. and upcoming vaccination research. Expanding the investigation of HIV-1 variability across nations at the full-length genome level while accounting for epidemiological variables is crucial.

CONCLUSIONS

The two main processes influencing HIV-1 genomic diversity are mutation and recombination. A huge monitoring challenge is the ongoing appearance of novel recombinant forms. It is essential to track HIV-1 variation and spread throughout Africa in order to comprehend the potential influence of these strains on AIDS. methods for diagnosis, therapy, and intervention.

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