Review Article

HIV Genotype Landscape in Bangladesh: A Comprehensive Overview

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This review offers a detailed examination of the HIV genotype landscape in Bangladesh, emphasizing the prevalence and distribution of HIV-1 subtypes and recombinant forms. The study aggregates findings from multiple sources to highlight subtype C as the predominant strain among infected populations, particularly among high-risk groups such as intravenous drug users and female sex workers. Additionally, it identifies other significant strains like CRF_07BC, CRF_01AE, and various recombinant forms, reflecting the genetic diversity of HIV in the region. The review underscores the importance of molecular epidemiology in shaping public health strategies, stressing the need for ongoing genotype surveillance to monitor transmission patterns and drug resistance mutations. Insights from this analysis advocate for tailored interventions that consider the specific genotype profiles prevalent in Bangladesh, aiming to optimize treatment outcomes and mitigate the spread of drug-resistant strains. The study concludes with a call for continued research to deepen understanding of genotype-specific impacts on disease progression and to inform targeted approaches in the management and prevention of HIV in Bangladesh.

1. Introduction

Background on HIV and its global impact

The global impact of HIV has been a significant concern in the field of public health. Various studies have highlighted the prevalence of HIV and its implications on AIDS progression, response to antiretroviral therapy, and mortality rates[1]. The genetic differences among HIV-1 subtypes have also been identified as critical factors affecting clinical management and drug resistance surveillance, especially as antiretroviral treatment expands to regions where diverse non-subtype-B viruses are

predominant[2]. Estimating mortality, antiretroviral therapy needs, prevention of mother-to-child transmission impact, and uncertainty bounds are essential components in projecting the spectrum of HIV/AIDS at national and global levels[3]. Additionally, the implementation of global plans to combat diseases like tuberculosis and HIV involves optimizing allocations and assessing the contributions of organizations like the Global Fund to improve treatment outcomes and reduce mortality rates[4]. Expanded HIV treatment has shown promise in preventing AIDS-related deaths, as evidenced by trends in AIDS deaths, new infections, and antiretroviral therapy coverage in countries with high AIDS mortality burdens[5]. Academic institutions have also played a crucial role in the global response to the HIV pandemic, with programs like PEPFAR emphasizing the transition to local ownership for sustainability and capacity building[6]. The global COVID-19 pandemic has raised concerns about its potential impact on the transmission dynamics and prevention of HIV and other sexually transmitted infections, highlighting the need for continued research and modeling to understand these implications[7]. Cost-effectiveness analysis has been utilized to prioritize interventions in HIV, tuberculosis, and malaria, providing valuable insights for decision-makers in resource allocation and program planning[8]. In conclusion, understanding the background of HIV and its global impact is crucial for developing effective strategies to combat the spread of the virus, improve treatment outcomes, and reduce mortality rates worldwide. Ongoing research and collaboration among various stakeholders are essential to address the challenges posed by HIV and other infectious diseases on a global scale.

Importance of understanding HIV genotypes

Understanding HIV genotypes is crucial in the context of HIV/AIDS research and prevention efforts. Leclerc-Madlala[9] emphasizes the importance of focusing research on mediating environments that nullify safe-sex messages, highlighting the need for a deeper understanding of HIV genotypes to inform effective interventions[9]. Maughan-Brown[10] discusses the stigma associated with HIV/AIDS, indicating that understanding different genotypes of the virus could potentially impact attitudes toward individuals living with the disease[10]. Heath et al.[11] conducted a study comparing HIV-1 genotypes in breast milk and plasma, revealing the presence of CXCR4 co-receptor using viruses in both tissues[11]. This finding underscores the significance of understanding the distribution of different genotypes in various bodily fluids. Altfeld et al.[12] discuss the dysregulation of the immune response in HIV-1 infection and highlight the importance of comprehending how HIV affects immune

cells like dendritic cells (DCs) and natural killer (NK) cells[12]. This understanding is crucial for developing effective antiviral strategies. Saxena et al.[13] emphasize the importance of understanding the bacterial component of HIV/AIDS and the potential crosstalk between viral and bacterial pathogens[13]. This underscores the need to comprehend the role of different genotypes in the context of the human microbiome. Akinbo et al.[14] detected and genotyped Enterocytozoon bieneusi in HIV-infected individuals, showcasing the diversity of genotypes present in this population[14]. Ng et al. [15] provide insights into the phylodynamic profiles of HIV-1 genotypes circulating among men who have sex with men (MSM) in Kuala Lumpur, Malaysia[15]. This study highlights the importance of understanding transmission behaviors and evolutionary history in assessing the risk of outbreak or epidemic expansion. Montgomery et al.[16] discuss the influence of male partners on women's participation in HIV prevention trials, emphasizing the importance of understanding various factors, including genotypes, in shaping prevention strategies[16]. Gabrielaite et al.[17] found associations between human leukocyte antigen (HLA) alleles and HIV variants, indicating the impact of host genetics on viral genotypes[17]. Jing et al.[18] present a metapopulation model to predict the geographical spread of a new HIV genotype among MSM in Guangdong, China, highlighting the importance of considering genotypes in the control and prevention of HIV[18]. Overall, the literature underscores the importance of understanding HIV genotypes in various contexts, from influencing attitudes toward HIV/AIDS to shaping prevention strategies and assessing transmission dynamics[19]. This knowledge is essential for developing targeted interventions and improving outcomes in the fight against HIV/AIDS.

2. HIV Genotypes Overview

Explanation of HIV-1 and HIV-2

The Human Immunodeficiency Virus (HIV) is a complex virus that has two main types, HIV-1 and HIV-2. Research has shown distinct differences between these two types of virus. One study by Arya et. al., (1988) analyzed the regulatory elements of the long terminal repeat of HIV-2, revealing the presence of two functionally independent TAR elements[20]. This finding suggests that HIV-2 *Tat* requires the presentation of two viral RNA stem-loop sequences for full activity, unlike HIV-1 *Tat* which is maximally active with a single stem-loop structure[21]. Further comparative analyses have been conducted to understand the differences between HIV-1 and HIV-2. Garrett et. al., 1992

compared the *Rev* function in both types of the virus[22], while Cock et. al., 1993 explored the epidemiology and transmission of HIV-2, highlighting why there is no HIV-2 pandemic[23]. Additionally, Marlink et. al., 1994 conducted a study that demonstrated a reduced rate of disease development after HIV-2 infection compared to HIV-1, indicating that HIV-2 has reduced virulence[24]. Studies have also investigated the impact of HIV-1 and HIV-2 on cellular processes[25]. Wang et. al., 2009 examined changes in apoptosis-related proteins in Jurkat cells infected with either HIV-1 or HIV-2, finding that the expression of certain proteins inhibited HIV replication[25]. Alford et. al., 2016 discovered that HIV-2 *Gag* is trafficked in an AP-3 and AP-5-dependent manner, shedding light on differences in particle production between HIV-1 and HIV-2[26]. Moreover, research has explored the interactions between HIV-1 and HIV-2. Sahin et al. (2013) identified frequent intratype neutralization by plasma immunoglobulin A in HIV-2 infection, suggesting differences in neutralizing activity between HIV-1 and HIV-2[27]. Mahdi et. al., 2018 investigated the inhibitory effects of HIV-2 *Vpx* on the replication of HIV-1, proposing that interference at the viral accessory/regulatory protein level may contribute to the attenuated pathogenicity of HIV-1 in dually infected patients[28]. Overall, these studies provide valuable insights into the differences between HIV-1 and HIV-2, shedding light on the distinct characteristics and behaviors of these two types of the virus[29]. Further research is needed to fully understand the mechanisms underlying these differences and their implications for the development and treatment of HIV infections.

Subtypes and recombinant forms of HIV

The genetic diversity of human immunodeficiency virus (HIV) has been a topic of interest in various regions around the world. Studies have shown that in West Africa, India, and certain parts of Europe, both HIV-1 and HIV-2 are known to cocirculate, leading to investigations into the subtypes involved in dual infections[30]. Additionally, research in Thailand has identified novel recombinant forms of HIV-1, such as CRF01_AE and subtype B, transmitted heterosexually among individuals in the region[31]. The emergence of recombinant forms of HIV has also been observed in Malaysia, with the identification of CRF33_01B and CRF74_01B among people who inject drugs (PWIDs) in Kuala Lumpur[32][33]. Furthermore, studies have highlighted the genetic complexity of HIV-1 in Southeast Asia, particularly in Malaysia, where the expansion of CRF33_01B among PWIDs has been noted, along with the emergence of multiple unique recombinant clusters[34]. In South-East Asian patients infected with CRF01_AE and subtype B, transmission clusters have been identified, emphasizing the

importance of using genotypic data to quantify local epidemics[35]. In Europe, the molecular epidemiology of HIV-1 has been studied to understand the characteristics and evolution of the epidemic over time, providing insights into the spread and growth of the virus in the region[36]. Similarly, in China, research has focused on the prevalence, temporal trends, and geographical distribution of HIV-1 subtypes among men who have sex with men, highlighting the importance of monitoring subgroups based on study time period and sampling area[37]. Moreover, investigations in Shenzhen, China, have revealed the characteristics of genotype, drug resistance, and molecular transmission networks among newly diagnosed HIV-1 infections, showcasing the diversity of HIV-1 subtypes in the region[38]. Overall, these studies underscore the importance of understanding the genetic diversity and transmission dynamics of HIV-1 to inform prevention and treatment strategies in different populations and regions.

3. Global Distribution of HIV Genotypes

Prevalence of different HIV genotypes worldwide

A summary is depicted in Table 1 for the global distribution of HIV-1 subtypes[39].

This table provides a broad overview of common distribution trends and global occurrence. Regional prevalence and exact proportions may differ.

HIV-1 Subtype	Description	Global Prevalence
Subtype A	Primarily found in East Africa and certain regions of Eastern Europe.	Prevalent in East Africa and Russia
Subtype B	Most prevalent in North America, Western Europe, and certain areas of Latin America.	Common in North America and Europe.
Subtype C	Most widespread globally, with significant prevalence in Southern Africa and India.	Extremely prevalent in Southern Africa and India.
Subtype D	Mainly found in East and Central Africa.	Moderate prevalence in East Africa.
Subtype F	Present in South America and select regions of Europe.	Low to moderate prevalence in South America and Europe.
Subtype G	Found in West and Central Africa.	Low to moderate prevalence in West Africa.
Subtype H	Rare, primarily found in Central Africa.	Uncommon.
Subtype J	Present in Central and South America, though relatively uncommon.	Uncommon.
Subtype K	Extremely rare, with only a few identified cases.	Very rare.
CRF (Circulating Recombinant Forms)	Recombinant forms result from combining different subtypes; prevalent in various regions.	High prevalence in Southeast Asia and Africa.

Table 1. Global distribution of HIV-1 subtypes

Human immunodeficiency virus (HIV) is a diverse virus that can be classified into two main types: HIV-1 and HIV-2. HIV-1, the predominant type worldwide, accounting for 95% of cases, is further divided into four groups: M, N, O, and P[40].

Group M, the most common, includes nine subtypes (A to K), with Subtype C being the most prevalent globally, particularly in southern Africa, east Africa, and India, making up 46.6% of cases between 2010 and 2015[40]. Subtype B is the main subtype in the United States and other regions like North

America, South America, Europe, Australia, the Middle East, and northern Africa[40]. Subtypes F, H, J, and K have a combined prevalence of only 0.9%. On the other hand, HIV-2 is mostly found in western Africa, divided into nine groups (A to I), with groups A and D currently circulating in humans[40].

HIV-2 transmits less effectively, progresses more slowly, and is resistant to some antiretroviral drugs such as non-nucleoside reverse transcriptase inhibitors (NNRTIs)[40]. The virus is known for its ability to mutate, creating different strains within subtypes. Superinfection, where an individual contracts multiple strains, can complicate treatment, especially if the new strain is resistant to current drugs[40]. Additionally, the recombination of subtypes can lead to the creation of hybrid viruses known as circulating recombinant forms (CRFs), with 157 identified so far, highlighting the complex and evolving nature of HIV[41].

Factors influencing HIV genotype distribution

The distribution of HIV genotypes is influenced by a variety of factors, including geographical location, migration patterns, and public health initiatives. Geographical location plays a critical role as certain genotypes, such as HIV-1 Subtype C, are more prevalent in specific regions like southern Africa, while Subtype B is more common in North America and Europe[42]. Migration and travel can introduce different HIV genotypes into new areas, altering the local distribution. Additionally, public health initiatives, including HIV prevention and treatment programs, can impact genotype distribution by affecting transmission rates and the effectiveness of antiretroviral therapies. For instance, widespread use of certain antiretroviral drugs can be selected for resistant strains, thereby influencing the genotypic landscape[43]. Socioeconomic factors, such as healthcare access and education, also play significant roles, as they determine how well populations can implement prevention strategies and access treatment[44]. Therefore, understanding the multifaceted influences on HIV genotype distribution is crucial for tailoring effective public health strategies.

4. HIV Epidemiology in Bangladesh

This systematic review investigates the molecular epidemiology of HIV-1 in Bangladesh, emphasizing the importance of such studies in resource-limited settings with significant migrant populations[45]. The review aims to summarize findings on HIV-1 subtype prevalence in Bangladesh. Researchers retrieved articles from six databases using keywords related to HIV-1 subtypes and Bangladesh,

ultimately including five studies with pooled sequences from 317 individuals. The results show that subtype C is the most prevalent (51.10%), followed by CRF_07BC (15.46%), CRF_01AE (5.68%), A1 (4.73%), CRF_02AG (3.47%), G (3.15%), CRF_62BC (2.84%), B (2.21%), and other subtypes in smaller percentages. Subtype C is predominant among intravenous drug users and female sex workers, while the migrant population exhibits a diverse range of subtypes due to travel to the Middle East and Southeast Asia[46] and Table 2]. The study concludes that with rising HIV-1 infections and an increasing migrant population, detailed molecular epidemiological data are essential to manage and mitigate the HIV-1 epidemic in Bangladesh.

Sl#	Subtype Name	No of sequence	Collection Year	Author
1	01_AE	20	2002-2004; 2013,2019	Sarker, M.S; Rahman, S
2	02_AG	18	2001;2004;2005;2006; 2013;2016;	Sarker, M.S; Rahman, S
3	06_cpx	8	2005-2007;	Sarker, M.S;
4	07_BC	1	2019	Molla, M.M.A
5	09_cpx	4	2005-2006;	Sarker, M.S
6	13_cpx	1	2006;	Sarker, M.S
7	15_01B	1	2020	Rahman, S
8	16_A2D	7	2006	Sarker, M.S
9	22_01A1	1	2019	Rahman, S
10	25_cpx	3	2006-2007	Sarker, M.S
11	43_02G	1	2006	Sarker, M.S
12	65_cpx	1	2019	Rahman, S
13	A	4	2001;2007	Ljungberg, K; Sarker, M.S
14	A1	29	2001-2007;2016;2019	Ljungberg, K; Sarker, M.S; Rahman, M
15	A1G	1	2003	Sarker, M.S;
16	A2	2	2006	Sarker, M.S;
17	B	5	2002;2004;2007	Sarker, M.S;
18	C	461	2001-2009;2012-2016;2019	Ljungberg, K; Sarker, M.S; Rahman, S Molla, M.M.A
19	D	2	2004	Sarker, M.S
20	G	19	2001-2003;2005-2007	Sarker, M.S; Ljungberg, K
21	U*	2	1991	Ljungberg, K
	Total	591		

Table 2. HIV-1 subtypes circulating in Bangladesh

*One is subtype D and the other is subtype A based on genotyping tools [https://www.ncbi.nlm.nih.gov/projects/genotyping/genotype.cgi]

5. Impact of HIV Genotype on Disease Progression

The genotype of HIV significantly impacts disease progression, influencing the rate at which the virus replicates and the severity of the infection. Different HIV genotypes and subtypes exhibit varying levels of virulence and immune system evasion capabilities. For instance, studies have shown that individuals infected with HIV-1 Subtype D tend to experience faster disease progression compared to those infected with Subtype A[47]. Similarly, HIV-1 Subtype C, which is prevalent in many parts of Africa and India, is associated with a slower progression to AIDS compared to other subtypes[48]. The presence of recombinant forms, which combine genetic material from different subtypes, can further complicate disease progression due to their unique replication dynamics and resistance profiles[49]. Additionally, the variability in genetic sequences among different HIV strains can affect the effectiveness of antiretroviral therapies, leading to treatment challenges and the necessity for genotype-specific treatment strategies[50]. Therefore, understanding the impact of HIV genotype on disease progression is crucial for developing targeted therapeutic approaches and improving patient outcomes.

6. Drug Resistance and HIV Genotypes

Association between specific genotypes and drug resistance

The association between specific HIV genotypes and drug resistance is a critical area of study, as it directly impacts the effectiveness of treatment regimens. Certain genotypes have inherent resistance to specific classes of antiretroviral drugs. For instance, HIV-1 Subtype C, prevalent in regions such as southern Africa and India, has been linked to a higher propensity for developing resistance to non-nucleoside reverse transcriptase inhibitors (NNRTIs)[51]. This subtype's genetic makeup allows it to more readily develop mutations that confer resistance to these drugs, complicating treatment strategies. Similarly, recombinant forms like CRF_02AG, which are common in West Africa, have

shown diverse resistance patterns due to their mixed genetic backgrounds, making them more challenging to treat with standard regimens. In a study involving 33 subjects, with a median age of 34.5 years, who had been on antiretroviral therapy (ART) for a median of 12 months, 41.7% of the successfully genotyped viruses possessed at least one mutation conferring resistance to nucleoside or non-nucleoside reverse-transcriptase inhibitors (NRTIs/NNRTIs). Two-class drug resistance to NRTI and NNRTI was detected in 25% of the cases. The most frequent mutations were lamivudine-resistance M184V and efavirenz/nevirapine-resistance K103N. Notably, HIV-1 subtype CRF_02AG was predominant (79.2%), with other subtypes like G (8.3%), A3 (4.2%), and unique recombinant forms with CRF_02AG/A3 mosaic detected[52]. The presence of these resistant strains highlights the need for ongoing surveillance and the development of genotype-specific treatment approaches to ensure that therapies remain effective across different populations. Understanding these associations not only aids in tailoring treatments but also underscores the importance of personalized medicine in managing HIV.

Prevalence of drug-resistant strains in Bangladesh

In Bangladesh, antiretroviral therapy (ART) is initiated without prior screening for drug resistance-associated mutations (DRM) among HIV-positive individuals, potentially allowing DRM to develop and spread among newly infected individuals. This study aimed to assess DRM prevalence among ART-naive clients at an HIV testing and counseling (HTC) center in the early stages of ART programs. Using archived plasma samples from 64 randomly selected clients, the *pol* gene was amplified and sequenced. Ten sequences were successfully genotyped using NCBI tools and analyzed with the Stanford University HIV drug resistance database. The study identified various genotypes with DRM, indicating resistance to drugs like tipranavir/ritonavir (10 out of 10), albeit with some variability in resistance levels. Despite the limited sample size, the findings underscore the need for Bangladesh to implement an ART policy integrating DRM monitoring to optimize treatment outcomes and limit the spread of drug-resistant HIV strains[53].

7. HIV genotypes and Implications for Treatment and Care

The diversity of HIV genotypes has profound implications for treatment and care strategies, influencing both the effectiveness of antiretroviral therapy (ART) and the management of drug resistance. Different genotypes exhibit varying responses to treatment regimens, necessitating

personalized approaches tailored to specific viral strains. For instance, HIV-1 Subtype C, prevalent in regions like southern Africa and India, is associated with certain resistance mutations that may affect treatment outcomes[54]. Understanding these genotype-specific resistance profiles is crucial for selecting appropriate first-line and salvage therapies to maximize viral suppression and prevent treatment failure. Moreover, the emergence of recombinant forms, such as CRF_02AG, which combine genetic material from different subtypes, poses additional challenges in treatment due to their unique resistance patterns and transmission dynamics[55]. Therefore, comprehensive genotype testing and ongoing surveillance are essential to inform treatment decisions and ensure effective long-term management of HIV, particularly in diverse epidemiological settings like Bangladesh.

8. HIV Genotypes and Research Gaps and Future Directions

Research on HIV genotypes has made significant strides in understanding viral diversity and its implications for transmission, treatment, and resistance. However, several research gaps remain that warrant attention in future studies. One crucial area is the exploration of genotype-specific differences in disease progression and treatment outcomes across diverse global populations. Understanding why certain genotypes, such as HIV-1 Subtype C or recombinant forms like CRF_02AG, predominate in specific regions and their impact on epidemic control is essential[56][57]. Additionally, more research is needed on the dynamics of recombinant viruses and their potential to evade immune responses and antiretroviral therapies. Improving genotype surveillance methods, particularly in resource-limited settings, is critical for the early detection of emerging drug resistance mutations and the development of effective treatment strategies tailored to regional genotype profiles. Furthermore, investigating the role of host genetics in influencing HIV genotype susceptibility and disease outcomes could provide insights into personalized medicine approaches. Addressing these gaps will not only enhance our understanding of HIV epidemiology but also inform public health policies and interventions aimed at achieving global HIV control and elimination goals.

9. Policy Implications

Understanding HIV genotyping findings can significantly inform national HIV/AIDS policies by providing crucial insights into the epidemiological landscape and guiding strategic interventions. For instance, identifying prevalent HIV genotypes and their associated drug resistance patterns can aid policymakers in tailoring treatment guidelines and procurement strategies for antiretroviral drugs

(ARVs). Countries can prioritize procurement of ARVs that are effective against locally prevalent genotypes, thereby maximizing treatment outcomes and minimizing the development of drug resistance. Moreover, genotype surveillance can help monitor the emergence of new drug-resistant mutations and guide adjustments in treatment protocols and public health strategies accordingly. Policymakers should prioritize investments in genotype testing infrastructure and capacity building to ensure timely and accurate surveillance data. Recommendations include fostering collaboration between public health authorities, researchers, and healthcare providers to establish standardized protocols for genotype testing and interpretation. By integrating genotyping data into national HIV/AIDS programs, policymakers can enhance treatment effectiveness, optimize resource allocation, and ultimately advance toward achieving HIV epidemic control goals.

10. Conclusion

The article underscores the critical importance of understanding HIV genotypes in the context of Bangladesh's epidemiological landscape. Highlighting the predominance of HIV-1 subtype C and various recombinant forms among different risk groups, the review emphasizes the necessity for robust molecular epidemiological data to inform targeted HIV prevention and treatment strategies. The findings underscore the challenges posed by diverse HIV genotypes, including their implications for drug resistance and disease progression. Recommendations include integrating genotype surveillance into national HIV/AIDS policies to optimize treatment outcomes and mitigate the spread of drug-resistant strains. Future research directions should focus on addressing gaps in genotype-specific disease dynamics and enhancing surveillance methods in resource-limited settings. Overall, the article calls for collaborative efforts among researchers, policymakers, and healthcare providers to effectively manage and control the HIV epidemic in Bangladesh.

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