Genetic Diversity and Drug Resistance Patterns among HIV-1 Positive Youths with Non-Suppressed Viral Load in South Rift Valley, Kenya

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Abstract

Background: Globally, Human immunodeficiency virus (HIV) is a leading cause of morbidity and mortality. The fundamental Antiretroviral Therapy (ART) goal is to curb the spread of HIV and enhance the survival of HIV infected patients. Despite the tremendous benefits of ART, HIV treatment and management failures among the youth have been attributed to non-adherence to drug regimens and viral mutations leading to the emergence of drug resistance. Therefore, this study aimed to determine the genetic diversity and HIV-1 drug resistance patterns among the youth aged 15-24 years with non-suppressed viral load in the South Rift Valley Region (SRV), Kenya.

Methods: A cross-sectional study design was adopted to select a total of 120 plasma samples from HIV-1-positive youth who had been on different ART regimens for over six months. Remnant plasma samples with >1000 copies/ml from real-time PCR using the Abbott Real-Time HIV-1 m2000rt quantitative kit were sequenced using the HIV-1 genotyping kit with integrase between April 2024 and October 2024. The target genes were Reverse Transcriptase, Protease and Integrase of the *pol gene*. HIV-1 level of drug resistance was evaluated using the Exatype Sanger analysis tool. Mutation patterns were ascertained by analysing FASTA files using the drug resistance HIV Stanford database. The subtypes of HIV-1 were analysed by the REGA HIV subtyping tool, and Maximum-likelihood phylogenetic trees and annotations of the mutations were constructed using the integrated Tree of Life.

Results: Sequencing was completed for 99 samples, and *Tenofovir Disoproxil Fumarate* + *Lamivudine* + Dolutegravir (TDF/3TC/DTG) was the most commonly prescribed antiretroviral regimen across all age groups. The predominant HIV subtype was A1 (83%). Drug resistance was attributed to mutation, M184V (31.4%) associated with resistance to *Emtricitabine* and *Lamivudine*, K103N (20.9%) and G190A (15.1%) resistance to *efavirenz*, *nevirapine* and *rilpivirine*, G118R (5.7%) to *raltegravir*, *elvitegravir* and *bictegravir*.

Conclusion: There was high genetic diversity of HIV-1 among the youths aged between 15 and 24 years, and subtype A1 is the dominant circulating form of HIV-1 in the South Rift Valley region. Understanding the evolutionary relationships of these strains provides insights into their genetic diversity and transmission.

Keywords: *HIV-1 Positive, Non-suppressed Viral Load, Genetic Diversity, Drug Resistance*

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Introduction

HIV-1 is a human immunodeficiency virus (HIV), which has three basic enzymes: Reverse-transcriptase (RT), Integrase (IN), and Protease (PI) (1). HIV-1 has four groups of phylogenetic classifications: O (outlier),

M (major), N (non-M/non-O), and P. The global epidemic is attributed to the M group, which makes up more than 95% of the HIV-1 positive samples sequenced globally. Group M is further classified into nine other subtypes (J, A–D, K, F–H), two Fs (F1 and F2), and A1 to A6, besides the other 102 forms of circulating recombinants. Genetic diversity is strongly correlated with the drug resistance pattern of the HIV-1 strain (2). In Northern Brazil, for instance, the Transmitted Drug Resistant (TDR) HIV-1 strain negatively impacted the outcomes of Antiretroviral therapy (ART) and highly active antiretroviral therapy (HAART), leading to treatment failures observed within the HIV-1 infected patients (3). A phylogenetic tree denotes a graphical species evolutionary characterisation of relationships, and the species phylogenetic diversities that indicate the evolutionary closeness of their relationships (4). Therefore, understanding the evolutionary relationships of these strains provides insights into their genetic diversity and transmission.

In several Sub-Saharan African countries, increased resistance to pretreatment drugs extends to non-nucleoside reverse transcriptase inhibitors (NNRTIs) and protease inhibitors (PIs). A study in Nigeria associated drug resistance of HIV-1 against common anti-retroviral therapy regimen to mutations in Integrase Strand Transfer Inhibitor (INSTI) and Circulating Recombinant Forms (CRT02) of the virus (5). In 2018, the WHO approved the transition to dolutegravir, an INSTI with an in-penetrable barrier to resistance as a component of an induction ART in resource-scarce situations (5). INSTIs targeting the integrase (IN) enzyme critical to HIV replication have shown enhanced treatment efficacy among naïve and seasoned patients (6). Globally, INSTIs have been widely adopted as a first-line treatment critical for those living with HIV and clinical research has demonstrated that INSTIs are comparatively superior to PI and NNRTI treatment groups (7). Notably, for the second generation INSTIs, amino acid substitutes G193E, R263K, E92Q, S153FY, and G118R decrease Dolutegravir (DTG) vulnerability up to two to four times. M50I seems likely to be preferred in vitro by Bictegravir (BIC) and DTG with R263K in combination, thus leading to reduced DTG vulnerability (8).

In Ethiopia, a study to ascertain the relationship between drug resistance and genetic diversity among HIV-1 patients on various anti-retroviral therapy regimes revealed that 85.4% of the sampled patients exhibited at least one type of Acquired Drug Resistance (ADR) mutations (9). Previous studies have pointed out a few NRTI and NNRTI-associated mutations responsible for drug resistance among HIV-1 patients on anti-retroviral treatment, for instance, a study reported that 81% and 48.8% of patients exhibited resistance to Nucleoside Reverse Transcription Inhibitor and Non-Nucleoside Reverse Transcriptase Inhibitors, respectively (10). Consequently, a significant obstacle hindering the long-term achievement of ART efficacy is the development of resistance (11). In resource-scarce settings, lack of proper adherence is the major factor contributing to drug resistance and subsequent failure in treatment among these vulnerable patients (12). Some important NRTI related mutants identified in China are 184VF, 65R, Y115F, K70E, Q41L, D67N, K219N while those associated with NNRTI were E138AG, V179ED, K101EQ, 106MI, Y181C, G190A, K103N and 227L (13).

The genetic diversity of HIV-1 in Kenya has been widely studied, for example,

in Teso, Western Kenya. The analysis of HIV-1 diversity among patients on antiretroviral therapy indicated that 68% of cases were subtype A1, while 12.7% were subtype D8. Inter-subtype recombinants were observed as well, with A1-D3 at 4.8% and A1-B2 at 3.2% (14). Moreover, a study conducted in Nairobi among treatment-experienced HIV-1 patients reported drug resistance mutations; the NRTI-related mutations were M184VI & K65REN, while those of NNRTI, K103NS, G190A and Y181 (15).

A recent study highlighted a higher Virologic Non-suppression (VNS) (25%) among the younger demographic (18-24 years) compared to the general HIV-positive population in coastal Kenya (16). To date, few studies on genetic diversity and drug resistance patterns of HIV-1 among Kenyan youth undergoing anti-retroviral treatment have been conducted. Therefore, we aim to determine drug resistance and genetic variability patterns of HIV-1 among youth aged 15-24 years on Anti-Retroviral Therapy in the South Rift region of Kenya.

Materials and Methods

Study design and site

The study utilised a laboratory-based cross-sectional study design to analyse drug resistance in HIV-1 samples. This study was nested in the ongoing National STI &AIDS Control Programme (NASCOP), Kenya Ministry of Health, funded by the Presidential Emergency Plan for AIDS Relief (PEPFAR).

The study utilised the remnant coded plasma samples selected on a real-time basis from HIV-1 patients with a viral load of >1000 copies/ml measured by the m2000rt Abbott Real-Time quantitative assay at the Walter Reed Project laboratory in Kericho, and the results were dispatched through the NASCOP database to health facilities.

Study population

The plasma remnant samples were identified from the youths enrolled in the NASCOP for HIV-1 viral load monitoring. The inclusion criteria included youths aged between 15 and 24 years who had been on ART for more than 6 months, with a Viral Load of > 1000 copies/ml. Youths with incomplete regimen records and youths who had been on ART for a period of more than 6 months with a viral load of > 1000 copies/ml but not enrolled on the ongoing National STI &AIDS Control program were excluded from the study.

Sampling size and techniques

The sample size for this study was computed using Cochran's formula for sample size determination, embracing a 95% level of confidence. 118 was the sample size.

$$n = \frac{Z^2 P(1\text{-}P)}{e^2}$$

Where n: is the required sample size, Z: is the z-score associated with the desired confidence level, 1.96 for 95% confidence, p: was the estimated proportion of the population that possesses the characteristic of interest 8.4% derived from a previous study conducted in Kenya by Scriven YA *et.* al, (16) e: was the desired margin of error or level of precision (0.05).

$$n = \frac{1.96^2 \times 0.084(1-0.084)}{0.0025} = 118$$

The sample size was rounded up to 120 to facilitate balancing at stratification. We used stratified sampling to ensure fair regional distribution, and purposive sampling was used to enrol the desired age group and viral load quantities. These methods ensured geographical diversity while capturing the specific qualities required for the study.

Overview of laboratory tests

HIV genotyping. HIV genotyping of protease, reverse transcriptase, and integrase was performed using the HIV-1 genotyping

kit with integrase by Thermo Fisher Scientific. This kit is designed to detect HIV genomic mutations in the Protease codons 6-99, Reverse transcriptase codons 1-251, and Integrase codons 1-288 regions of the pol gene in RNA isolated from human immunodeficiency virus type 1. Briefly, RNA was extracted from 200 µL of plasma using a PureLink™ Viral RNA/DNA Mini Kit, according to the manufacturer's instructions. The extraction yielded 50 µL of RNA; 10 µL of extracted RNA, along with a positive and negative control, were reverse transcribed and amplified by polymerase chain reaction (PCR), which was performed for each region using two µL of amplified DNA. DNA amplicons were verified by gel electrophoresis and purified using ExoSAP-IT (Thermo Fisher Scientific). Using Platinum Taq DNA Polymerase (Thermo Fisher Scientific, Waltham, US). Forward primer Pro1 (TAGAGCCAACAGCCCCACCA, HXB2: 2147 -2166) and reverse primer 5066R (ATCATCACCTGCCATCT GTTTTCCAT, HXB2: 5041–5066) were used in the nested PCR. Afterwards, Sanger sequencing reactions were performed using six primers (F1, F2, F3, R1, R2, R3) for PR/RT and four primers (F11, F12, R11, R12) for IN; 2 µL of purified DNA was used for each reaction. To amplify a ~ 4 kb HIV-1 *pol* region, SuperScript IV One-Step RT-PCR System (Thermo Fisher Scientific, Waltham, US), forward primer PANA2AF (GAGGCAATGAGCCAARCAAACA, HXB2: 1882–1903) and reverse primer PANA3AR (TTCCAGGGCTCTAGKTTAGG, HXB2: 5846–5865) were used in One-Step RT-PCR. Cycle sequencing products were purified using the BigDye XTerminator Purification Kit (Thermo Fisher Scientific) and analysed by capillary electrophoresis using the Applied Biosystems 3500xL Genetic Analyzer (Thermo Fisher Scientific). Software-guided editing and manual editing were performed, and consensus sequences (FASTA files) were generated.

Analysis of HIV drug resistance for NRTIs, NNRTIs, PIs, and INSTIs was performed using the Stanford HIV Drug Resistance Database (v9.5.0). For this analysis, FASTA files from the HIV-1 genotyping kit with integrase were uploaded to "Input sequences" with the output options of "sequence summary" and "resistance summary". Data were categorised by HIV subtype, RAMs detected, and predicted HIV drug resistance.

Sequence analysis and phylogenetics. Following capillary electrophoresis, sequence editing was performed using the Exatype™ Platform. Assessed HIVDR mutations using the Stanford University HIV drug resistance database (version 9.5). Phylogenetic analysis was performed for paired PR/RT and IN sequences generated by the HIV-1 genotyping kit with integrase. Multiple pairwise sequence alignment was performed using MEGA version 12. An annotation of the mutations was constructed using the integrated Tree of Life (iTOL) with maximum likelihood tree reconstruction with 1000 bootstrap replicates. HIV subtypes were obtained using the Stanford HIV Drug Resistance Database (v9.5.0).

Data analysis

The derivative data was keyed into Microsoft Excel software. Cleaning and review of the data were constantly undertaken in Microsoft Excel. To determine genetic diversity, a REGA HIV subtyping tool was used. The subtype HIV-1employs the MEGA4 software neighbour-joining method (19).

The HIV-1 *pol* gene mutations were calculated using the HIV-1 by Stanford drug resistance HIV Database (1), and validated utilising the updated 2019 International AIDS Society–United States, drug resistance mutations in HIV-1 (20). The Drug Resistance Mutations(DRMs) were classified further using the algorithm described in the Stanford HIV-1 drug resistance database, with levels designated as high, intermediate, low, potential low-low resistance, and susceptible.

Ethical considerations

Ethical clearance was obtained from the University of Kabianga, Kenya Medical Research Institute Scientific and Ethical Unit (KEMRI-SERU) and Walter Reed Army Institute of Research (WRAIR) institutional review boards (IRBs) (ISERC/2023/0004) and WRAIR#3113, respectively. The National Commission of Science and Technology, Kenya (NACOSTI) (Ref #.455975) granted the approvals.

Results

Virological parameters

A total of 120 remnant samples were tabulated for virological parameters. (Table 1). From the results, *the Tenofovir Disoproxil Fumarate* + *Lamivudine* + Dolutegravir regimen was the most used at 89.2%(n=107), females at 90% (n=69) and males 84.4% (n=38), followed by *Abacavir* + *Lamivudine* + Dolutegravir for males at 6.7% (n=3).

Treatment duration among females was evenly distributed, with 33.3% receiving ART for more than six months to two years and a similar proportion for more than two to five years (n = 25). Among males, the highest proportion (37.8%) had been on treatment for over five to eight years (n = 17). The viral load levels at 1,001 to 9,999 copies/ml were at 50.7% (n=38) for females and 60% (n=27) for males.

Table 1

Demographic and Virological Parameters of 120 Remnant Plasma Samples

Parameters		Female, N = 75	Male, N =45
Age strata (Yr)	15-16	7(9.3)	7(15.6)
	17-18	13(17.3)	11(24.4)
	19-20	13(17.3)	15(33.3)
	21-22	16(21.3)	7(15.6)
	23-24	26(34.7)	5(11.1)
Treatment duration (yrs)	>6 months - 2 yrs.	25(33.3)	5(11.1)
	>2 yrs. - 5yrs	25(33.3)	7(15.6)
	>5 yrs. - 8 yrs	16(21.3)	17(37.8)
	>8yrs - 12yrs	9(12)	11(24.4)
ART regimen	TDF+3TC+DTG	69(92)	38(84.4)
	AZT+3TC+LPV/r	2(2.7)	1(2.2)
	AZT+3TC+DTG	0(0)	1(2.2)
	ABC+3TC+LPVr	1(1.3)	1(2.2)
	TDF+3TC+ATVr	1(1.3)	0(0)
	ABC+3TC+ATVr	0(0)	1(2.2)
	ABC+3TC+DTG	0(0)	3(6.7)
	AZT+3TC+ ATV/r	2(2.7)	0(0)
Viral loads(cp/m/)	1001 - 9999	38(50.7)	27(60)
	10,000 - 99,999	27(36)	13(28.9)
	100,000 - 999,999	10(13.3)	5(11.1)

***Key: ABC** -Abacavir, **3TC**- Lamivudine, **DTG**-Dolutegravir, **LPV/r**-Lopinavir/Ritonavir, **AZT**- Zidovudine, **ATV/r**-Atazanavir/Ritonavir, **TDF**- Tenofovir Disoproxil Fumarate*

Genetic Diversity HIV-1 subtyping

Genetic variability analysis using regions encoding a portion of the *env-gp41* protein of HIV-1 among youth aged 15-24 years from the 99 samples that managed to sequence successfully. From the results, it shows that 83% (n=80) were subtype A1, 8% (n=8) were subtype C, and 9 %(n=9) were subtype D from the REGA subtyping tool v3.46.

Drug resistance mutation pattern

Sequencing was successful for 99 samples. Of these, 74 yielded sequences for both the reverse transcriptase, protease and integrase genes. In total, 86 samples were successfully sequenced for the reverse transcriptase, protease gene, and 88 samples for the integrase region.

In the results, the mutation frequency, M184V, was the most prevalent mutation at 31.4% while T215Y (5.8%), T215F (5.3%) and L74I (4.7%) were less frequent, and T125A and S68G in the NRTIs occurred at less than 4%. Looking at the NNRTI drugs, K103N (20.9%) and Y181C (15.1%) were the most common mutations, while E138A (9.3%) and K103S (4.7%) were less common. In the PI class, M461 and 154L occurred at very low frequencies for the INSTI class; the mutations were similarly low, with E138K and T66A occurring at low frequencies.

Table 1

Distribution of HIV-1 Subtypes among the Study Participants

HIV Subtypes	Female (N=62)	Male (N=37)	Percentage (%)
Subtype A	56	26	83
Subtype C	2	6	8
Subtype D	4	5	9

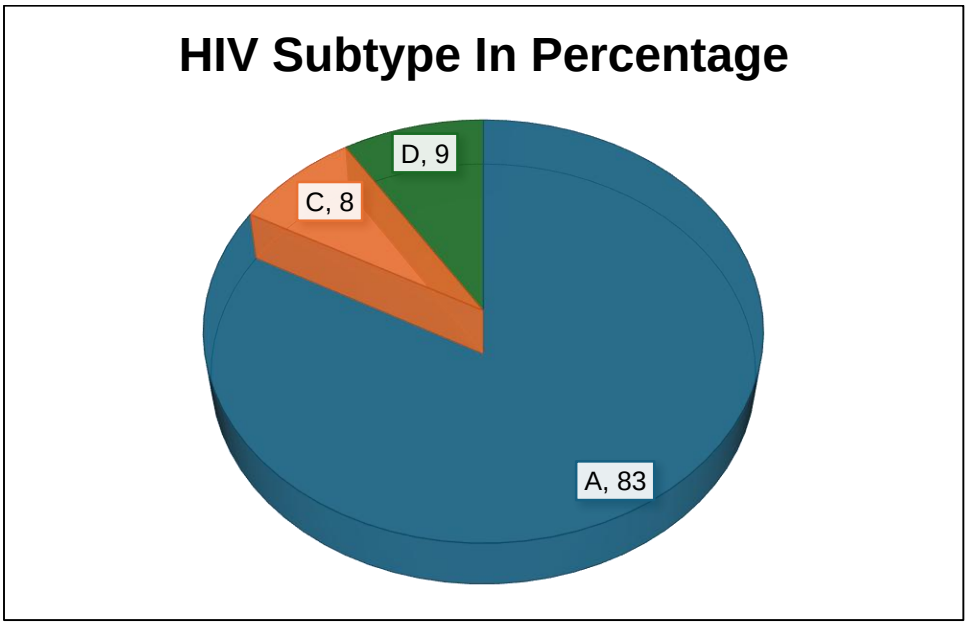

Figure 1

Distribution of HIV-1 subtypes among the Study Participants

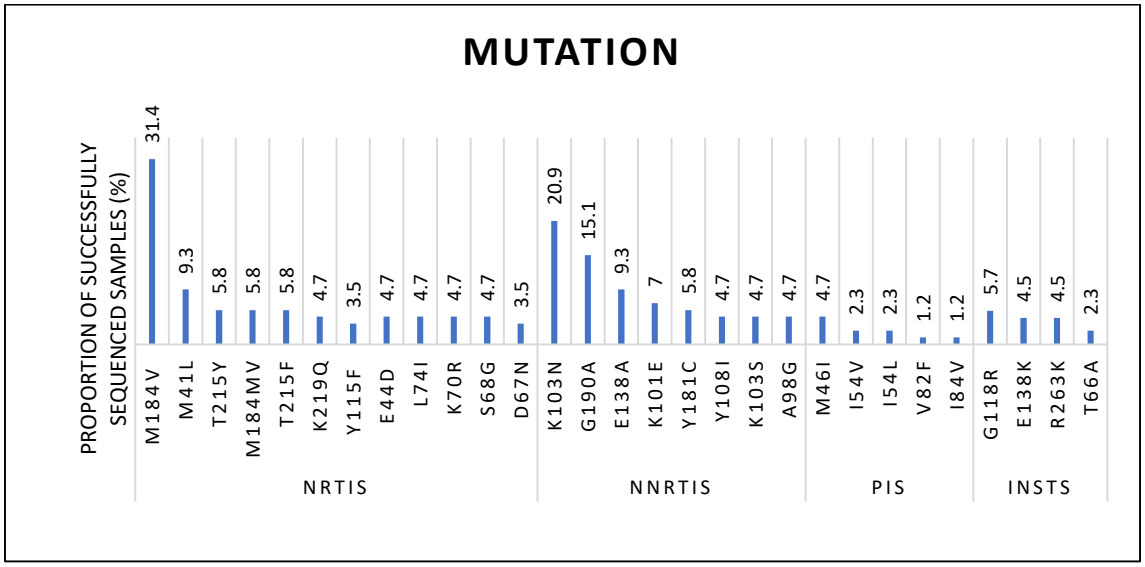

Figure 2

Mutation pattern among youth aged 15-24 years in the South Rift Valley region in Kenya NNRTIs- non-nucleoside reverse transcriptase inhibitors, NRTIs- Nucleoside reverse transcriptase inhibitors, PIs- Protease Inhibitors, INST- Integrase Inhibitors

Table 2

Resistance Patterns Associated with ARV Drug Classes

	High-Level Resistance	Low-Level Resistance	Intermediate - Low Resistance	Potential Low-Level Resistance	Susceptible
Reverse Transcriptase NRTIs					
(ABC)	12	8	12	0	54
(AZT)	14	0	0	1	71
(FTC)	31	0	0	0	55
(3TC)	31	0	0	0	55
(TDF)	1	8	9	1	67
Reverse Transcriptase NNRTIs					
(DOR)	5	5	4	7	65
(EFV)	31	11	0	1	43
(ETR)	8	7	4	13	54
(NVP)	42	1	0	0	43
(RPV)	15	5	12	0	54
Protease Inhibitors					
(ATV/r)	1	1	5	1	78
(DRV/r)	0	1	2	0	83
(LPV/r)	1	1	3	3	78
Integrase Inhibitors					
(BIC)	4	4	0	1	79
(CAB)	8	0	1	0	79
(DTG)	5	3	0	1	79
(EVG)	6	2	1	3	76
(RAL)	5	2	2	3	76

BIC - *bictegravir,* CAB- *cabotegravir,* EVG- *elvitegravir,* RAL- *raltegravir, emtricitabine (FTC), doravirine (DOR), efavirenz* (EFV), *etravirine* (ETR), *nevirapine* (NVP), *darunavir/r* (DRV/r),

The NNRTI class had high resistance to *nevirapine* 48.8% (n=42/86), followed by *efavirenz* 36%(n=31/86). For NRTIs, high resistance to both *emtricitabine* and *lamivudine* 31/86, PIs had intermediate low resistance to *atazanavir/r (n=5),* and Integrase class had high resistance to *cabotegravir* 8/88 followed by *elvitegravir* 6/88. The susceptibility for protease inhibitors was 96.5% *for darunavir/r* (n=83/86), *atazanavir/r* and *lopinavir/r* was 90.7% There was no Low, intermediate or potential low for both *emtricitabine* and *lamivudine.*

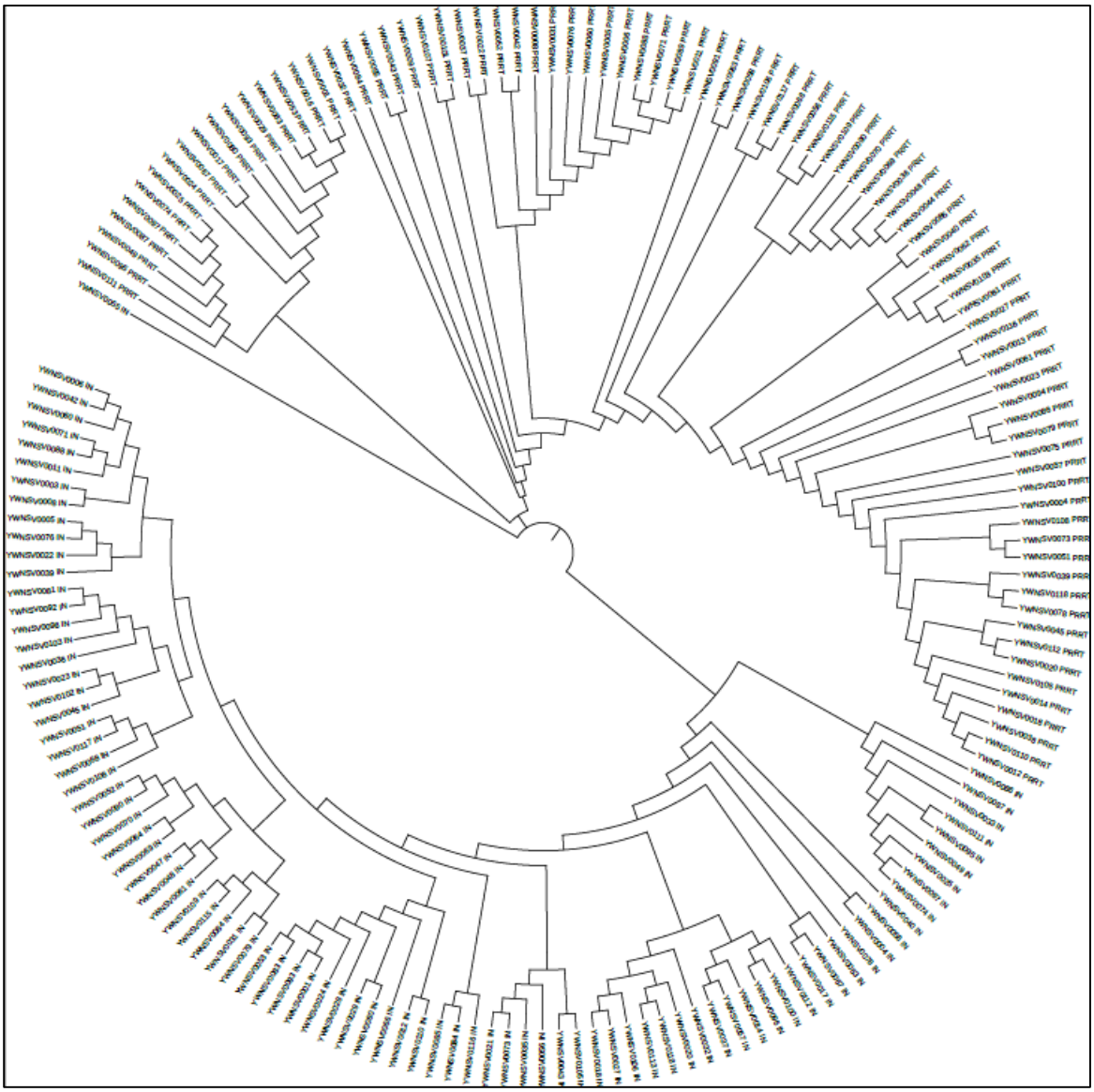

Figure 1

Phylogenetic Tree using Interactive Tree of Life Version 7.2.1(Aa-PxJjpJejRkzX9) Letunic I et.al,.2021) (17, 18). The clustering of samples could indicate a pattern among Lineages from the same (Homogeneous), which indicates a close ancestry. There are samples with multiple mutations that inferred resistance to all three classes of drugs.

Discussion

Findings from this study showed that the regimen *Tenofovir Disoproxil Fumarate* + *Lamivudine* + Dolutegravir regimen was commonly used among the youths, which demonstrated compliance with the recommended first-line regimen (29). Interestingly, this study confirmed that some youths (>10), although on the correct regimen, had a very high viral load (100,000 – 999,999 cp/ml), which could be attributed to poor adherence to the treatment. Based on prior studies, poor adherence to ARV drugs can be attributed to medication formulation and palatability, frequency of dosing, side effects, and drug toxicities (31). The advantages of initiating DTG/3TC include reduced short-term and long-term toxicity secondary to reduced cumulative ART exposure, fewer drug–drug interactions, and possible metabolic advantages (32). The efficacy of an antiretroviral therapy (ART) regimen depends on the activity of its individual antiretroviral drugs. When mutations confer resistance to two drugs within a triple-drug regimen, the regimen may fail to suppress HIV-1 replication, leading to poor clinical outcomes, including death (33).

The study characterised three subtypes that were pure. The predominant subtype was A1, then D, and lastly C in that hierarchical order, which is consistent with findings elsewhere (24,14). According to our findings, the most common HIV-1 subtype was subtype A1genotype (83%), followed by subtype C (8%) and subtype D (9 %). The contribution of HIV subtypes to the emergence of drug resistance has received increased attention. Globally, intensification of drug resistance to ART has been linked to subtype A1 (69.8%), followed by subtypes D (18.7%) and C (11.5%) (34).

The major mutation was on M184V, which has been associated with high-level resistance to two widely used nucleoside reverse transcriptase inhibitors: *lamivudine* and *Emtricitabine*. The two drugs are a first-line regimen that could render them ineffective, and this could explain the non-suppression among the study population. (27)

Additionally, K103N confers high-level resistance to many first-generation NNRTIs, including *efavirenz* and nevirapine. The drugs are a mainstay of initial HIV treatment regimens, and the resistance could be a major contributor to non-suppression of viral load. The G190A mutation confers high-level resistance to *nevirapine* and intermediate resistance to *efavirenz*. These two are widely used as first-line NNRTIs, especially in resource-limited settings. The high drug resistance to the class of NRTIs and NNRTIs necessitated the introduction of second-generation integrase strand transfer inhibitors such as dolutegravir (28). The guidelines advocate for the use of INSTI-based ART as the preferred treatment to be administered to those living with HIV (29). Antiretroviral drugs suppress but do not eliminate HIV infection. Mutations occur, reducing suppression of HIV-1 replication with currently available antiretroviral drugs (35).

Consistent with the literature, we observed NRRT mutations such as K103N, Y181C and G G190A clustering together, indicating a potential transmission or evolution of the resistant genes (1). The occurrence of multiple thymidine analogue mutations and M184V has been associated with drug resistance and poor treatment outcomes (25). Other findings showed a modest number of INSTI mutations such as G118R, E138K and R263K in some samples, suggesting emerging resistance to INSTI

resulting in reduced susceptibility to some drugs such as Dolutegravir (26).

Numerous clinical studies have confirmed that PI and NNRTI are less superior to the INSTIs groups as far as where comparative treatment is involved (30). HIV-1 drug-resistance testing plays a role in the management of HIV. However, there is a concern due to HIV drug-resistant mutations, which weaken the effectiveness of the drug (29). The integral component of HIV treatment has at least two combinations of NRTIs, and another being the third drug from NNRTIs, INSTIs or PIs. Information in this study plays a role in strengthening the health systems in the Country.

Study Limitations

Sequences used in this study were from patients enrolled in treatment programs and may not represent the full diversity of the circulating strains in the country. Additionally, the phylogenetic analysis based solely on the pol gene can only capture recombination events that occurred within or near that gene. It completely misses recombination events that may have occurred in other parts of the genome (e.g., *gag* or *env* genes) (37).

Conclusion

The high genetic diversity of HIV-1 among the youths aged between 15 and 24 years, and subtype A1 are the dominant circulating form of HIV-1 in the South Rift Valley region. Understanding the evolutionary relationships of these strains provides insights into their genetic diversity and transmission. Drug resistance testing is a critical tool to identify why the antiretroviral therapy (ART) isn't working and to guide the selection of a new, effective regimen. The goal is to determine which drugs the virus has become resistant to, allowing clinicians to build a new regimen with active drugs.

Recommendations

Continuous surveillance of subtypes and drug resistance is critical for informing public health policies, optimising treatment strategies, and guiding vaccine development efforts.

Genotypic HIV-1 resistance testing has become a tool for monitoring antiretroviral therapy. Combining pol gene analysis with other genomic regions like env or gag, and integrating it with epidemiological data, can improve the accuracy of inferred transmission histories. Therefore, laboratories should have a database containing *pol* gene sequences encompassing the protease (PR), RT region and Integrase region,

Abbreviations and definition of terms

ART - Antiretroviral therapy
DNA - Deoxyribonucleic acid
HAART - Highly active antiretroviral therapy
INSTIs - Integrase strand transfer inhibitors
NRTI - Nucleotide reverse transcriptase inhibitors
NNRTIs - non-nucleotide reverse transcriptase inhibitors
PCR - Polymerase chain reaction
PIs - Protease Inhibitors
RNA - Ribonucleic acid
VNS - Virologic non-suppressed
RT - Reverse Transcriptase
CRT02 - Circulating Recombinant Forms
TDR - Transmitted Drug Resistant
ssRNA - Single Stranded Ribonucleic Acid

Non-suppression. Denotes viral load >1000 copies/ml of blood established exactly 6 months after commencement of treatment.

Drug resistance. A situation where a drug in use is no longer effective and thus the pathogen proliferates despite its usage

Resistance pattern. A trend exhibited by antibiotic resistance for isolates testing results

Genetic Diversity. The genetic variability that is exhibited by organisms of the same species

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Authors' contributions

LC: study design, laboratory testing, data analysis and drafting of the manuscript. I.D. and J.K. Study design and manuscript review. All authors read and approved the final manuscript.

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Data Availability. The sequences have not been submitted to publicly available databases.

Conflict of interest statement. The authors declare that they have no competing interests

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