HIV Viral Suppression, Patterns of Drug Resistance Mutations and Correlates among Adolescents and Young Adults in the Context of Dolutegravir: A Cross-sectional Study in Tanzania

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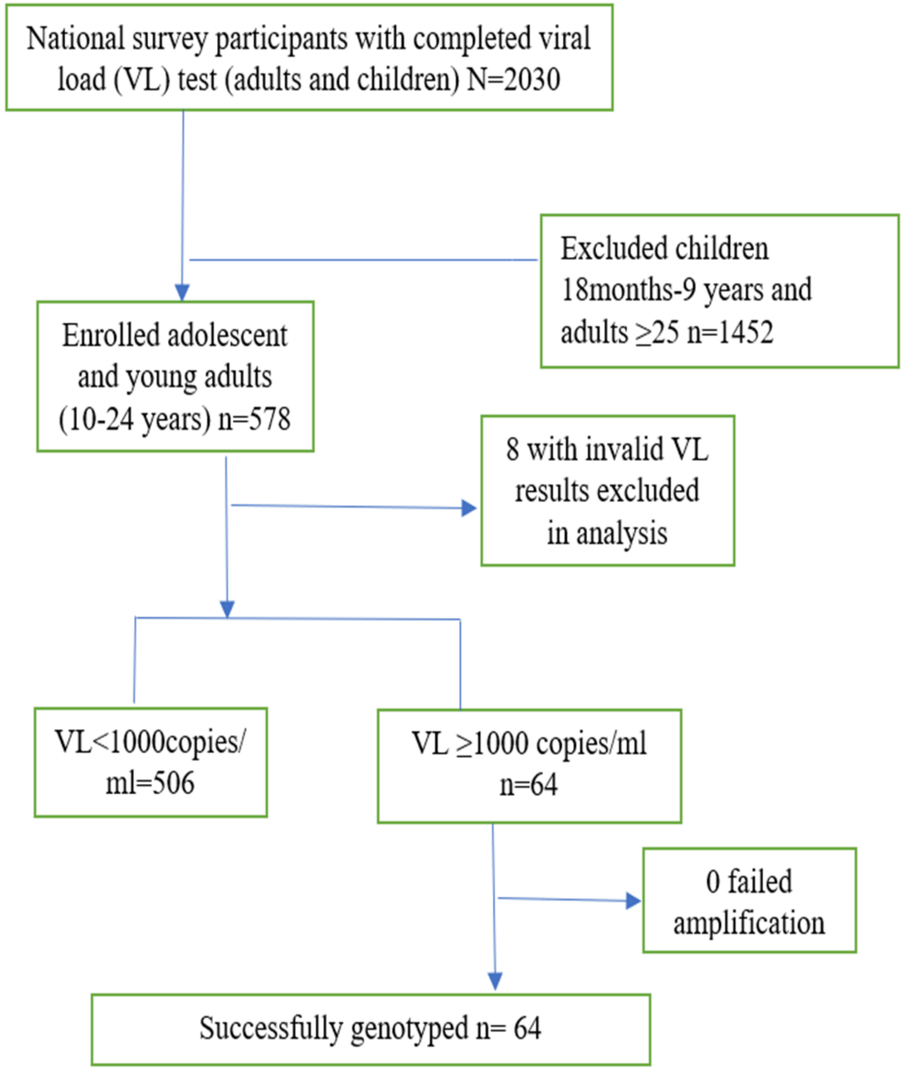
Introduction

- HIV drug resistance (HIVDR) remains a threat to the effectiveness of antiretroviral therapy (ART)
- HIVDR is a substantial barrier to reaching the UNAIDS Fast-Track goal of ending AIDS by 2030
- Drug resistance surveillance and drug susceptibility scores inform strategies for the implementation of effective ART
- Studies in sub Saharan Africa have reported higher rates of virologic failure among adolescents
    - assessing drug resistance in the context of a failing ART, provides clinical benefit and reduced mortality
- Tanzania had first acquired drug resistance (ADR) surveillance in 2020

Methods

- A cross sectional study of AYA 10-24 yrs nested in a national ADR surveillance
- Study sites: 36 facilities using a two-stage cluster design sampling
- Study period: July - October 2020
- WHO accredited laboratory in Canada for genotyping.
  - DBS samples
- HIV drug resistance was predicted using the Stanford HIV db algorithm.

Figure 1: flow chart study participants



Results

Table 1: Characteristics of Study Participants, N=570

Variable	Frequency (n)	Percent (%)
Age group (years)		
Adolescents (10 – 19)	535	92.6
Youth (20 – 24)	43	7.4
Sex		
Male	260	45.0
Female	318	55.0
Education		
No formal education	209	36.2
Primary education	324	56.1
O - level	43	7.4
A - level	1	0.2
Post-secondary	1	0.2
Median duration on ART in months (IQR)	66.0 (37.0, 100.0)	
ART regimen		
NNRTI based	15	2.8
PI based	68	12.9
INSTI based	444	84.3
HIV Viral Load (copies/mL)		
Suppressed (< 1000)	506	88.8
Non suppression (≥1000)	64	11.2

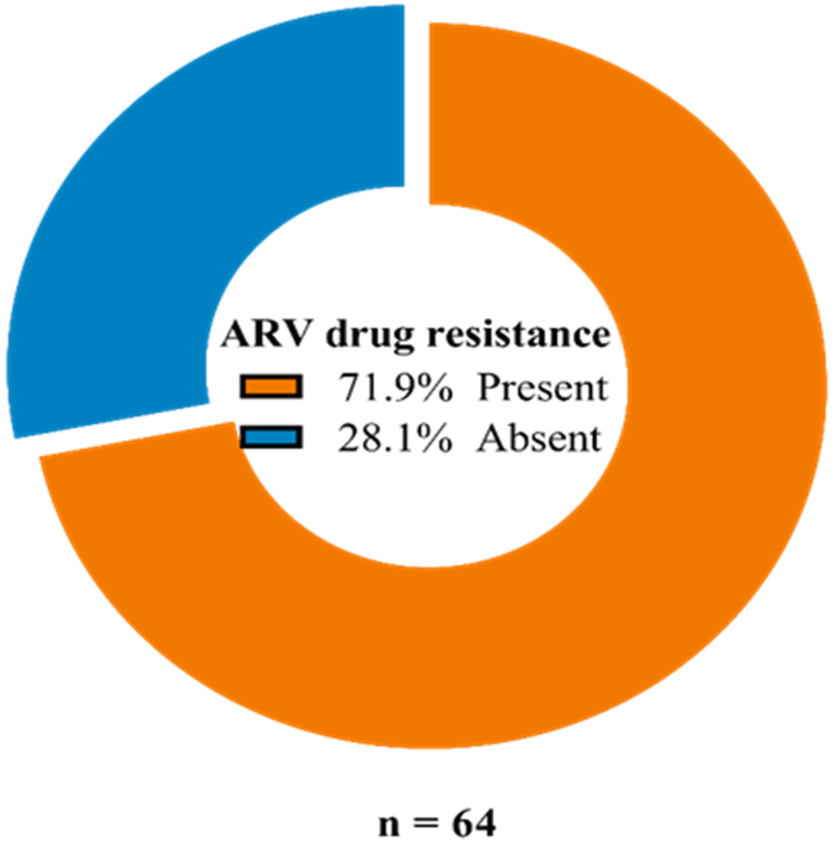
Results…

Non viral suppression (VL≥1000cp/ml)

- 64 participants were genotyped

Acquired drug resistance

- 71.9% had any drug resistance mutation (DRM)



Results : HIV drug resistance by ARV class

Fig 1: Frequency of drug resistance mutations by ARV classes

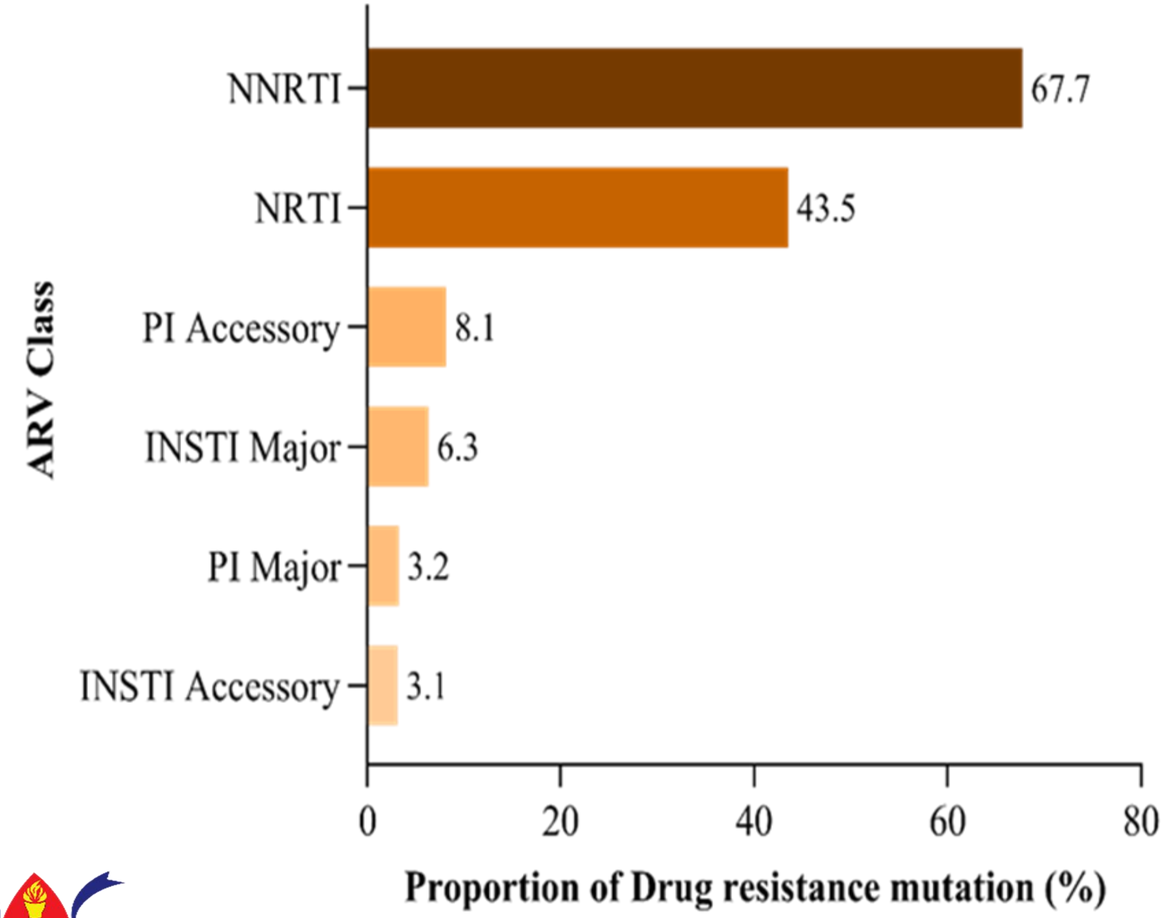
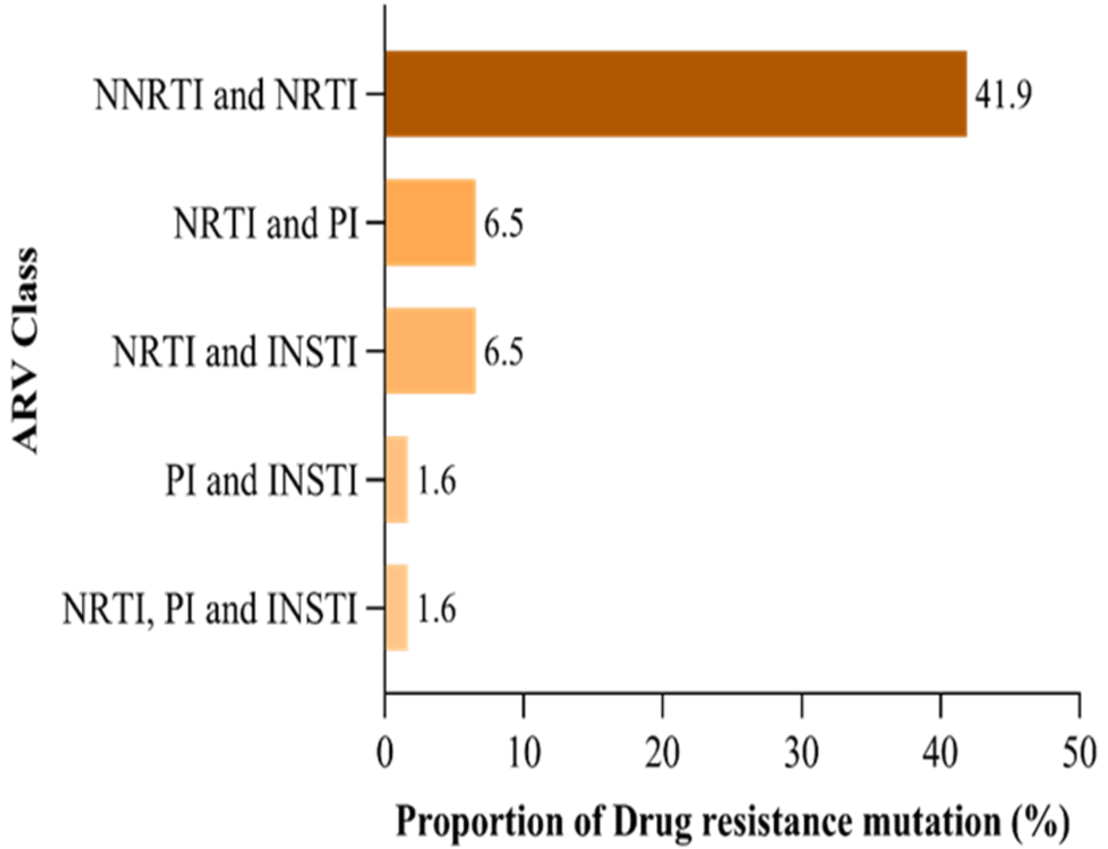


Fig 2: Proportion of dual class resistance by ARV classes



Clinically relevant HIV drug resistant mutations among AYA N=46

NNRTIs:K103N (42.9%)

NRTIs:M184V (42.9%),

Thymidine analogue mutations (TAMs): M41L (28.6%), T215Y/F (28.6%), L210W/L (14.3%), K70R (14.6%), D67N (14.6%)

NRTIs: ABSENT K65R

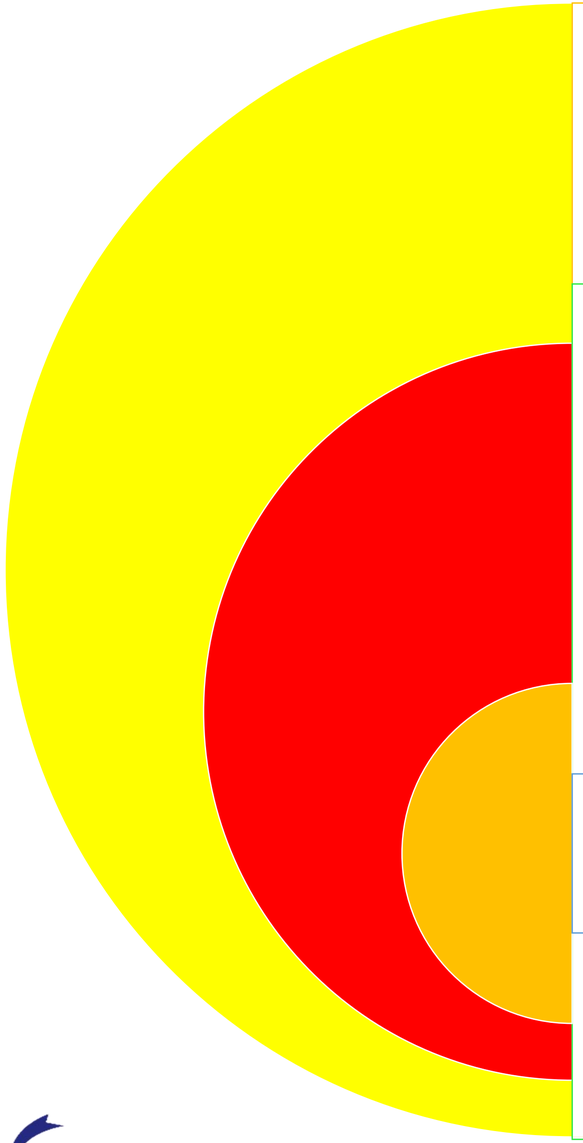
PIs: L89V/T (14.3%)

INSTI major:G118R, E138K, T66A and T97A (14.3%)

Factors associated with ADR among AYA

Variable	Anti-retroviral drug resistance		P - value
	Present (%)	Absent (%)	
Age group (years)			
10 – 14	39 (72.2)	15 (27.8)	1.000
15 – 24	7 (70.0)	3 (30.0)	
Gender			
Male	25 (83.3)	5 (16.7)	0.093
Female	21 (61.8)	13 (38.2)	
Education			
None	21 (75.0)	7 (25.0)	0.798
Primary	20 (71.4)	8 (28.6)	
Secondary	5 (62.5)	3 (37.5)	
Duration on ART (months)			
11 – 15	4 (57.1)	3 (42.9)	0.362
16 – 35	4 (57.1)	3 (42.9)	
>35	38 (76.0)	12 (24.0)	
Number of regimen change			
< 4	17 (63.0)	10 (37.0)	0.260
≥ 4	29 (78.4)	8 (21.6)	
Experienced side effects			
Yes	7 (87.5)	1 (12.5)	0.424
No	39 (69.6)	17 (30.4)	
Initial HIV viral load status			
Suppressed	12 (52.2)	11 (47.8)	**0.019**
Non-suppressed	34 (82.9)	7 (17.1)	
Latest CD4 count			
< 350	9 (81.8)	2 (18.2)	0.714
≥ 350	37 (69.8)	16 (30.2)	
Disclosure*			
Yes	35 (68.6)	16 (31.4)	0.307
No	5 (100)	0 (0.0)	
Adherence*			
Good	30 (70)	11 (26.8)	0.741
Poor	10 (66.7)	5 (33.3)	

Key discussion points



VS below UNAIDS target	• ADR survey > 70% of AYA were on DTG-based ART • existing AYA-friendly services need to address HIV care challenges that impair VS
71.9% had at least one DRM	• prolonged NNRTIs and NRTIs exposure - childhood • ↑NRTIs DRMs ↑risk for INSTI monotherapy • TAMs: prolonged treatment failure; AZT the subsequent NRTI in 2nd L ART; cross resistance; negative impact on TDF • Emerging INSTI DRMs-amplifying pre-existing INSTI • Low PI resistance
Initial VL≥1000copies/ml: a significant risk for DRMs	• Underscores optimal VL testing, early detection of high viremia and intervene to prevent ADR

Conclusion and recommendations

- More than one in ten AYA have high viremia in Tanzania
- A high prevalence of ADR and circulating DRMs calls for interventions to address prevention ADR
- A first HIV viral load test is a significant risk factor for developing HIV drug resistance.
- Genotypic testing during ART switch to guide the choice of NRTI backbone or recycled NRTIs to improve VS in the subsequent regimen
- Periodic national programmatic analysis of ART outcome data assessing on VS in young populations receiving TLD is crucial
- Evaluation of the implementation of differentiated service delivery (DSD) models for adolescents to improve VS

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