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RESEARCH

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Determinants of viral load non-suppression among HIV-positive children and adolescents attending care and treatment clinics in Tabora region, Tanzania

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Abstract

Background: In Africa, data on viral suppression among human immunodeficiency virus (HIV)-positive children and adolescents on antiretroviral (ART) are scarce. This study aimed to determine determinants of HIV viral load (VL) non-suppression among HIV-positive children and adolescents (< 20 years old) who attend care and treatment clinics (CTCs) in Tabora region from January 2018 to April 2022. Data were abstracted from CTCs' database and patient records including socio-demographic, ART drug regimen, clinical, virological and immunological features, for a maximum of 52 months. Viral non-suppression was defined as plasma VL ≥ 1000 copies/mil after 6 months on ART, during the follow-up period. Cox proportional hazards regression model and hazard ratios (HRs) were used in estimating the determinants of viral non-suppression.

Results: A total of 378 HIV-positive children (0–9 years) and adolescents (10–19 years) were enrolled, of whom 124 (32.8%) had virological non-suppression. The overall rate of VL non-suppression was 1.38 (95% CI 1.15, 1.64) per 100 person-months of observation. After adjusting for other factors, determinants of viral non-suppression were poor ART adherence level at initiation of ART (HR = 3.3; 95% CI 2.16, 4.91), low CD4 count at ART initiation (HR = 1.66; 95% CI 1.20, 2.30), nevirapine (NVP)-based regimen (HR = 2.64; 95% CI 1.32, 5.26), efavirenz (EFV)-based regime (HR = 2.08; 95% CI 1.03, 4.18), lopinavir/ritonavir (LPV/r)-based regimen (HR = 2.21; 95% CI 1.13, 4.32) and being on second-line regimen (HR = 6.11; 95% CI 2.50, 14.96).

Conclusions: HIV viral non-suppression among children and adolescents on ART in central Tanzania in the Tabora region is high (32.8%) and is associated with poor ART adherence level, low CD4 count, NVP-, EFV-, and LPV/r-based regimen. Early initiation of ART and intensified monitoring are required to improve viral suppression rates of HIV-infected children to attain the third goal of the UNAIDS 95-95-95.

Keywords: HIV viral non-suppression, ART, HIV infection, Children and adolescents, Tanzania

Background

In 2014, the Joint United Nations Programme on HIV and AIDS (UNAIDS) set motivated targets referred to as 95-95-95 aiming to control the HIV/AIDS epidemic by 2030 (UNAIDS 2021). The aim was that by 2030, 95% of all HIV-positive individuals knew their HIV status, whereby 95% of them are on ART, and 95% of all individuals on ART had suppressed viral load (VL) (UNAIDS

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2015). The basic premise of antiretroviral therapy (ART) is to attain maximal viral suppression, reduce the risk of transmission of HIV and improve the well-being of infected persons (WHO 2021). With the use of ART, mother-to-child transmission rates of HIV infection have dropped to less than 1% (UNAIDS 2019).

According to UNAIDS estimates, Tanzania had about 120,000 HIV-positive children at the end of 2017 (UNAIDS 2020a). In 2020 alone, Tanzania's HIV estimates suggested that there were 6500 new infections among children below 15 years (UNAIDS 2020b). According to the current guidelines, all these children should be enrolled in ART and monitored, primarily using VL measurements (NACP 2019a). Effective ART is essential in ensuring treatment, which is usually associated with significant viral suppression (WHO 2021).

However, many factors have been associated with VL non-suppression including poor ART adherence, low CD4 count, and co-morbidities in the adult population (Kahema et al. 2018). In this country, information regarding determinants of VL non-suppression among HIV-positive children and adolescents is limited. In this age group, adherence to ART is a challenge since they depend on parents and caregivers for access to care and treatment services (Somi et al. 2017). We conducted this study to determine the proportion and the determinants of viral non-suppression among HIV-positive children and adolescents on ART who attended the CTCs in the Tabora region. Determining factors of VL non-suppression amongst HIV-positive children and adolescents on ART will help HIV program administrators to adopt age-specific ART approaches that will be useful in reaching the third UNAIDS goal by 2030.

Methods

Study design

This was a retrospective follow-up study conducted between January 2018 and April 2022 among HIV-positive children and adolescents who were attending care and treatment clinics (CTCs) in Tabora, Tanzania.

Study site

The study was done in the Tabora region, which has seven councils, namely Tabora Municipal, Sikonge, Igunga, Kaliua, Uyui Urambo, and Nzega. The 2012 housing census reported 2291, 623 in the region. There is only one HIV VL testing Laboratory in the region, which is located at Kitete Regional Referral Hospital (RRH). We included all seven hospitals in the region, namely Kitete RRH, Igunga DH; Sikonge designated DH, Urambo DH, Nkinga mission hospital, Kaliua mission hospital, and Ndala hospital.

Study population

The study population comprised children (0–9 years) and adolescents (10–19 years) living with HIV who had been registered between January 2018 and April 2022 and were on ART for ≥ 6 months.

Inclusion criteria

All HIV-positive children and adolescents who were on ART for at ≥ 6 months were eligible for the study.

Exclusion criteria

Those who were lost to follow-up, died, transferred out and those whose files were not accessible were excluded from the study analysis.

Sampling method and sample size estimation

Sampling method

A simple random method was used to attain study participants. A list of CTCs in the Tabora region at the hospital level from seven districts was used. In a district with more than one hospital, a balloting method was applied; whereby the hospitals were assigned numbers, and the numbers were written on a different piece of paper and folded and then placed in a box and shaken thoroughly. Then, the hospital name from a selected piece of paper was included in the study. The seven selected CTCs are Kitete RRH, Igunga DH, Sikonge designated DH, Urambo DH, Nkinga mission hospital, Kaliua mission hospital, and Ndala hospital. The selected clinics represent geographical diversity, and significant numbers of HIV-positive patients attended CTCs in the region. In every selected CTC, HIV clients (aged < 20 years) and on ART for ≥ 6 months were arranged and a unique identification number based on the registration was assigned (Fig. 1).

Sample size estimation

We calculated sample size based on data from an African cohort study conducted in Uganda, Kenya, Tanzania, and Nigeria showing the overall proportion of non-suppression to be 9% and an adherence level of 77% (Kiweewa et al. 2019). We used a two-sided 95% confidence interval, and a minimum detectable alternative of ± 5% was used to calculate the power of the study, which was set at 99.9% via Open-Epi Version 3.01. The resulting sample size was 378.

The sample size distribution per CTC facility

Figure 1 shows a scheme showing clients, including children and adolescents who were on ART during the study period. In brief, a total of 101,698 patients living with HIV were ever enrolled in seven CTCs in the

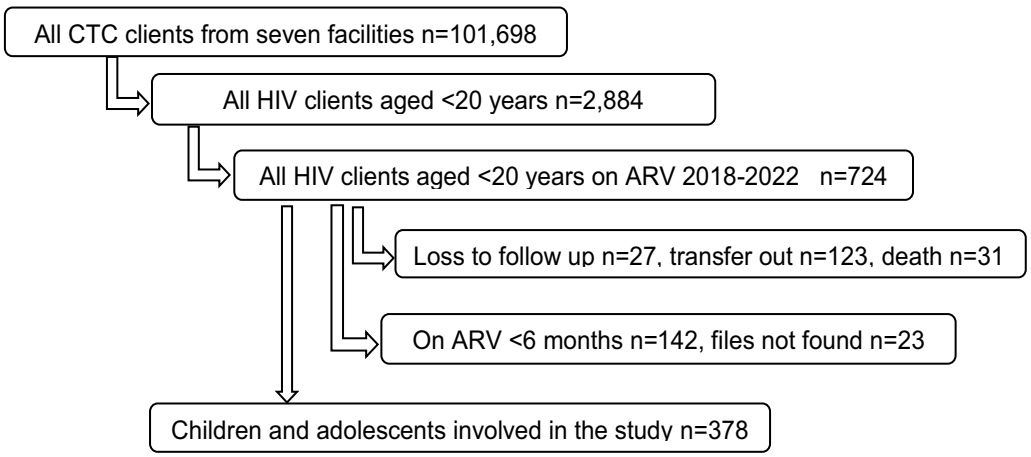

Fig. 1 A scheme showing the data of children and adolescents on ART

Tabora region, of whom 2884 were children and adolescents aged less than 20 years. Of the 2884 children, 725 children and adolescents were enrolled in ART. Of whom, 142 were not on ARV for at least six months, 23 files were not found, 27 were LTFU, 31 died and 123 were transferred out. All the remaining (378) client files were reviewed and included in the study analysis (Fig. 1). Their distribution per facility was as follows: Kitete RRH ($n=67$, 17.7%), Igunga DH ($n=61$, 16.1%), Sikonge designated DH ($n=40$, 10.6%), Urambo DH ($n=49$, 12.9%), Nkinga mission hospital ($n=50$, 13.2%), Kaliua mission hospital ($n=54$, 14.3%), and Ndala hospital ($n=54$, 15.1).

Data abstraction

Data were abstracted from the facility CTC database regarding the client's socio-demographic and clinical, ART drug regimen, and virological and immunological characteristics.

Dependent variable

The dependent variable was VL non-suppression. A binary outcome was categorized as non-suppression status or suppression status.

Independent variables

The independent variables were as follows: socio-demographic features (age, sex, education level, and HIV disclosure status). The regimen at the initiation of ART was categorized as (lopinavir/ritonavir (LPV/r)-based, dolutegravir (DTG)-based, efavirenz (EFV)-based, and nevirapine (NVP)-based (NACP 2019b). Adherence to ART treatment was categorized as 'good' and 'poor' according to the percentage of drug dosage calculated from the total monthly dose of ART drugs as follows: good (95% or ≤ 3 doses missed per month), or poor ($\geq 95\%$ or ≥ 4 doses missed per month) (NACP, 2019b). WHO clinical stage (categories; I, II, III, or IV)(WHO 2016). CD4 count was categorized as 'low' or 'high', low CD4 count was categorized as; CD4 count ≤ 350 cells/mm^3 for children above 5 years, and CD4% < 25% of total lymphocytes for children less than 5 years, and high CD4 count was categorized as; CD4 count > 350 cells/mm^3 for children above 5 years, and CD4% > 25% of total lymphocytes for children less than 5 years (NACP 2019b). Duration on ART of receiving HIV care and treatment in months, this was defined as: the time from initiation of antiretroviral (ARV) regimen (first or second line) to the date of data collection, death, loss to follow-up or transfer out, the categories of ART duration was; ≤ 2 years and > 2 years. Current ARV regimen (first-, second-line or third-line), and TB/HIV co-infection at the initiation of ART; 'yes' or 'no'. Completion of Isoniazid Preventive Therapy (IPT); categorized as 'yes' or 'no'. HIV disclosure status; categorized as 'Full disclosure', 'Complete non-disclosure' and 'Partial disclosure'. Full disclosure refers to providing the child or adolescent with the name of the diagnosis and full information and knowledge about HIV. 'Complete non-disclosure refers to maintaining complete secrecy around diagnoses, and the child or adolescent are not told the truth about their illness Partial disclosure is telling the child the truth, but not the whole truth, usually withholding the name of HIV (EGPAF 2016).

Pre-testing

Tool pre-testing was conducted on ten patient records with information from the CTC analytics database and medical records of children and adolescents HIV-positive and on ART for ≥ 6 months, registered in ART clinics

in the study period (January 2018–April 2022) at Kitete RRH.

Data processing and analysis

Data cleaning and analysis were performed using the STATA version 15 package (StataCorp. 2017. Stata Statistical Software: Release 15. College Station, TX: StataCorp LLC). Descriptive statistics were summarized using frequency and proportions for categorical variables, whereas continuous variables were summarized with a measure of central tendency with corresponding measures of dispersion. Incident rates were estimated, and a log-rank test was used to describe the survival experiences of categorical variables for the events of viral non-suppression. Bivariate analysis was done for all covariates. Hazard ratios (HRs) were estimated as a degree of association between viral non-suppression and client features, via a Cox proportional hazards regression. Variables with p-values less than 0.20 in the bivariate analysis were included in the multivariable analysis, whereas variables with a p-value ≤ 0.05 were measured as statistically significant determinants of viral non-suppression, with a 95% CI.

Results

Socio-demographic characteristics of the study participants

A total of 378 children and adolescents on ART were included in this study. Their median age was 6.0 (IQR 3,10) years and 126 (33.3%) were children (5–9 years old). More than half, 193 (51.1%) were male, and 231 (61.2%) were in either primary school or below (Table 1).

Table 1 Socio-demographic characteristics and HIV disclosure status of HIV-positive children and adolescents on ART in Tabora region, from January 2018 to April 2022 ($N = 378$)

Characteristic	Frequency (*N*)	Percent (%)
Sex		
Male	193	51.1
Female	185	48.9
Age (years)	Median, 6.0	(IQR 3,10)
Age at initiation of ART (Years)		
Less than 1	19	5.0
1–4	124	32.8
5–9	126	33.3
10–14	77	20.4
15–19	32	8.5
Education level		
None	21	5.6
Primary	210	55.6
Secondary	53	14.0
College/university	94	24.8
Districts		
Igunga	110	29.2
Tabora municipal	66	17.6
Nzega	58	15.3
Kaliua	54	14.2
Urambo	49	12.9
Sikonge	41	10.8
Disclosure of HIV status		
Full disclosure	43	11.4
Complete non-disclosure	147	38.9
Partial disclosure	188	49.7

Immunological and clinical characteristics of the study participants

Of the 378 HIV-positive children and adolescents enrolled in this study, 124 (32.8%) had virological non-suppression and 22 (5.8%) had TB/HIV co-infection, 139 (36.8%) had a WHO clinical stage III at the time of ART initiation and 205 (54.2%) had a high CD4 count (CD4 count > 350 cells/mm3 for children above 5 years, and CD4% > 25% of total lymphocytes for children less than 5 years) based on a national guideline for the management of HIV/AIDS (NACP 2019a). Among the total, 231 (61.1%) had disclosed their HIV status and 124(32.8%) were virological non-suppressed (Table 2).

Table 2 Immunological and Clinical characteristics of HIV-positive children and adolescents on ART in Tabora region, from January 2018 to April 2022 ($N = 378$)

Characteristic	Frequency (*N*)	Percent (%)
CD4 count/% at ART initiation		
High	205	54.2
Low	48	12.9
Missing	125	32.9
WHO stage at ART initiation		
I	121	32.0
II	105	27.8
III	139	36.8
IV	13	3.4
Active TB-status		
Yes	22	5.8
No	356	94.2

ART-related characteristics of the study participants

Regarding treatment regimen, 148 (37.2%) were on a dolutegravir-based regimen, 371 (98.2%) were in a first-line ART regimen, 224 (59.3%) had been on ART for more or equal to two years, 269 (70.8%) had good ART

Table 3 Drug regimen characteristics of HIV-positive children and adolescents on ART in Tabora region, from January 2018 to April 2022 ($N=378$)

Characteristic	Frequency	Percentage
Starting ART regimen		
DTG-based	148	37.2
EFV-based	59	14.8
LPV/r-based	127	31.9
NVP-based	64	16.1
Regimen line		
First-line	371	98.2
Second-line	7	1.8
ART adherence at ART initiation		
Good	269	70.8
Poor	111	29.2
Duration of ART (Years)		
< 2	154	40.7
≥ 2	224	59.3
Prevention treatment with Isoniazid (IPT)		
Yes	228	60.3
No	150	39.7

adherence status, 228 (60.3%) took Isoniazid preventive therapy (IPT) for TB (Table 3).

Virological suppression among HIV-positive children and adolescents on ART

Patients were followed for different periods with a total of 8,985 person-months (PM) of observations. A total of 124 (32.8%) patients developed viral non-suppression during the follow-up period. Hence, the overall rate of VL non-suppression was 1.38 (95% CI 1.15, 1.64) per 100 person-months (PM) of observations (Table 4). Non-suppression rates were higher among (i) male 1.7 per 100 PM (95% CI 1.36, 2.16) than female 1.1 per 100 PM (95% CI 0.80, 1.42), (ii) those not in school 2.9 per 100 PM (95% CI 1.70, 5.03) than those with diploma level 2.3 per 100 PM (95% CI 1.16, 3.09). The VL rates were 1.1 per 100 PM (95% CI 0.91, 1.51) for those attending primary schools and 0.5 per 100 PM (95% CI 0.25, 1.10) for secondary school attendees. As shown in Table 4, rates of non-suppressed VL were higher among those without tuberculosis 2.8 per 100 PM (95% CI 1.47, 5.44) than those with tuberculosis 1.4 per 100 PM (95% CI 1.10, 1.60), among those on second-line regimen was 6.3 per 100 PM (95% CI 2.84, 14.06) than those on first-line regimen 1.3 per 100 person-months (95% CI 1.11, 1.60). HIV VL non-suppression among those on LPV/r-based was 2.1 per 100 PM (95% CI 1.60,2.82) (Table 4).

Table 4 Virological suppression among HIV-positive children and adolescents on ART in Tabora region, from January 2018 to April 2022 ($N=378$)

Variable	Total (*N*)	Non-suppressed *n* (%)	Rate of non-suppression (per 100)	*p*-value
Non-suppression	378	124 (32.8)	1.36 (1.14,1.63)	
Sex				
Male	193	74 (38.3)	1.71 (1.36, 2.16)	0.007
Female	185	50 (27.0)	1.12 (0.80, 1.42)	
Age at initiation of ART (years)				
Less than 1	19	7 (4.76)	1.47 (0.70, 3.08)	
1–4	124	58 (26.3)	2.20 (1.70, 2.85)	
5–9	126	35 (30.4)	1.51 (0.83, 1.60)	< 0.001
10–14	77	16 (19.2)	0.83 (0.50, 1.36)	
15–19	32	4 (5.91)	0.68 (0.25, 1.80)	
Education level				
None	21	13 (61.9)	2.93 (1.70, 5.03)	
Primary	210	63 (30.0)	1.11 (0.91, 1.51)	< 0.001
Secondary	53	8 (15.1)	0.52 (0.25, 1.10)	
Diploma and above	94	40 (42.6)	2.33 (1.66, 3.09)	
Districts				
Igunga	111	32 (28.8)	1.33 (0.94, 1.87)	
Tabora municipal	67	21 (35.8)	1.17 (0.77, 1.80)	
Nzega	58	18 (31.0)	1.24 (0.78, 1.98)	0.952
Kaliua	54	18 (33.3)	1.59 (1.00, 2.52)	
Urambo	49	17 (36.9)	1.62 (1.01, 2.60)	
Sikonge	41	14 (36.6)	1.69 (1.00, 2.85)	
CD4 count/% at ART initiation				
High	205	149 (27.2)	3.71 (3.23, 4.25)	< 0.001
Low	48	24 (51.0)	5.57 (4.21, 7.38)	
Missing	122	44 (35.2)	5.39 (4.51, 6.44)	
WHO stage at ART initiation				
I	121	34 (28.1)	1.32 (0.92, 1.82)	
II	105	33 (31.4)	1.21 (0.86, 1.73)	
III	139	51 (36.7)	1.60 (1.21, 2.09)	0.178
IV	13	6 (46.2)	1.41 (0.59, 3.41)	
Active TB status				
No	356	115 (32.3)	2.84 (1.47, 5.44)	0.065
Yes	22	9 (40.9)	1.42 (1.10, 1.60)	
Regimen line				
First-line	371	118 (31.8)	1.31 (1.11, 1.60)	< 0.001
Second-line	7	6 (85.7)	6.32 (2.84,14.06)	
Starting ART regimen				
DTG-based	140	26 (18.6)	0.80 (0.53, 1.16)	
EFV-based	57	20 (35.1)	1.18 (0.76, 1.84)	< 0.001
LPV/r-based	118	50 (42.4)	2.12 (1.60, 2.82)	
NVP-based	63	28 (32.8)	1.61 (1.09, 2.32)	
Time on ARVs (years)				
< 2 years	154	40 (26.0)	1.70 (1.22, 2.33)	
≥ 2 years	224	84 (37.5)	1.31 (1.04, 1.60)	0.722

Table 4 (continued)

Variable	Total (*N*)	Non-suppressed *n* (%)	Rate of non-suppression (per 100)	*p*-value
Disclosure of HIV status				
Yes	43	15 (34.9)	1.51 (.088, 2.43)	
No	147	64 (45.5)	2.01 (1.56, 2.58)	0.001
Partial	188	45 (23.9)	0.92 (0.69, 1.24)	
ART adherence level at ART initiation				
Good	267	62 (65.4)	0.92 (0.71, 1.18)	
Poor	111	63 (21.3)	2.82 (2.19, 3.63)	< 0.001
Prevention treatment with Isoniazid (IPT)				
Yes	227	74 (33.1)	1.44 (1.10, 1.75)	0.888
No	151	50(32.8)	1.32 (0.99, 1.74)	

Determinants of HIV viral non-suppression

In the bivariate Cox proportional hazard regression analysis, sex, age, education level, ART regimen line, ART regimen-based, ART adherence level, and CD4 test results at ART initiation were significantly associated with VL non-suppression (Table 5).

In the multivariable analysis after adjusting for sex, age, education level, CD4 count at ART initiation, ART regimen-based, current regimen line, and ART adherence status, four factors including, ART adherence status, CD4 count at ART initiation, current regimen line and ART regimen-based, were significantly associated with viral non-suppression (Table 5). Children and adolescents with poor ART adherence levels compared to those with good ART adherence levels (HR = 2.82; 95% CI 2.19, 3.63). Those with low CD4 count had a higher hazard of viral non-suppressed compared to those with high CD4 count (HR = 1.66; 95% CI 1.20, 2.30), while those treated with NVP-based regimen had a higher hazard of viral non-suppressed compared to those with DTG-based regimen (HR = 2.64; 95% CI 1.32, 5.26). Compared to those with a DTG-based regimen those treated with LPV/r-based regimen had a higher hazard of viral non-suppressed (HR = 2.21; 95% CI 1.13, 4.32). Finally, those treated with a second-line regimen had a higher hazard of viral non-suppressed compared to those treated with a first-line regimen (HR = 6.11; 95% CI 2.50, 14.96) (Table 5).

Discussion

This study found a high HIV VL non-suppression proportion (32.8%) among HIV-infected children and adolescents who were on ART for at least six months, in Tabora region. The overall rate of non-suppression in this study was 1.4 per 100 PM observations and was

Table 5 Bi-variable and multi-variable analysis for determinants of HIV viral non-suppression among HIV-positive children and adolescents on ART in Tabora region, from January 2018 to April 2022 (*N* = 378)

Variable	CHR (95%CI) *p*-value		AHR (95%CI) *p*-value	
Sex				
Male	1		1	
Female	0.61 (0.44, 0.91)	0.008	0.86 (0.57, 1.30)	0.460
Age at initiation of ART (years)				
Less than 1	1			
1–4	1.50 (0.69, 3.29)	0.310		
5–9	0.81 (0.36, 1.82)	0.610		
10–14	0.58 (0.24, 1.41)	0.230		
15–19	0.41 (0.12, 1.40)	0.156		
Education level				
Nil	1		1	
Primary	0.41 (0.22, 0.75)	0.004	0.52 (0.26, 1.04)	0.065
Secondary	0.18 (0.07, 0.45)	< 0.001	0.28 (0.07, 1.03)	0.056
College/university	0.72 (0.38, 1.34)	0.299	0.61 (0.31, 1.23)	0.167
TB-status				
Yes	1			
No	1.72 (0.87, 3.40)	0.190		
Current regimen line				
First-line	1		1	
Second-line	4.83 (2.10, 10.94)	< 0.001	6.11 (2.50, 14.96)	< 0.001*
Starting ART regimen				
DTG-based	1			
EFV-based	1.80 (1.02, 3.32)	0.043	2.08 (1.03, 4.18)	0.040
LPV/r-based	2.72 (1.65, 4.35)	< 0.001	2.21 (1.13, 4.32)	0.021*
NVP-based	2.41 (1.39, 4.15)	0.002	2.64 (1.32, 5.26)	0.006*
ART adherence level at ART initiation				
Poor	3.12 (2.15, 4.41)	< 0.001*	3.31 (2.16, 4.91)	0.001*
Good	1		1	
WHO clinical stage at ART initiation				
I	1			
II	1.01 (0.64, 1.71)	0.860		
III	1.32 (0.83, 2.02)	0.247		
IV	1.42 (0.54, 3.58)	0.492		
Disclosure of HIV status				
Yes	1			
No	1.32 (0.76,2.36)	0.311		
Partial	0.61 (0.35, 1.14)	0.128		
Duration on ART				
< 2 years	1			
≥ 2 years	1.12 (0.74, 1.63)	0.632		
CD4 count /% at ART initiation				
High	1			
Low	1.85 (1.35, 2.53)	< 0.001*	1.66 (1.20, 2.30)	0.002*
Missing	1.96 (1.55, 2.48)	< 0.001*	2.01 (1.59, 2.54)	< 0.001*

*p-value < 0.05 statistically significant

significantly associated with poor ART adherence, NVP, EFV and LPV/r-based ARV regimen, second-line ART regimen, and low baseline CD4 count.

The non-suppression proportion (32.8%) found in this study is significantly lower than the third UNAIDS set goal of having a viral suppression of 95% among clients on ARVs (UNAIDS 2021). Our finding is consistent with studies conducted in Uganda and South Africa (30.2–31.4%) (Lilian et al. 2021; Maena et al. 2021), but high compared to the study conducted in Kenya (20%) (Mwangi and van Wyk 2021) and one in Uganda (23%) (Nabukeera et al., 2021). These variations might be due to differences in the quality of care in service delivery like counselling and adherence support activities (Nabukeera et al. 2021).

The association between poor adherence and low CD4 count with HIV viral load non-suppression found in this study is consistent with findings of other studies (Agegnehu et al. 2020; Hawkins et al. 2016; Waju and Dube 2021). High levels of ART adherence have been associated with better virological suppression as well as improved immunological and clinical outcomes (Giulia et al. 2019). This finding does emphasize the importance of early initiation of ART when CD4+ counts are still high and while the WHO clinical stage is favourable (Ruzicka et al. 2019). In this study, we found children and adolescents who were treated with a second-line regimen to be likely associated with viral non-suppressed, which is in keeping with the findings reported in Eastern Uganda (Maena et al. 2021) and those of an African Cohort study (Kiweewa et al. 2019) and several other studies (Afrane et al. 2021; Bulage et al. 2017; Chhim et al. 2018; Endebu et al. 2018; Giulia et al. 2019). The possible explanation is that such children had poor adherence to the first-line ART regimen, which may generally forecast poor adherence to the second-line ART regimen as well (Alene et al. 2019). The implication is that intensive adherence counselling is essential before clients are switched to other ARV regimens.

We found differences in HIV VL non-suppression on NVP-based ARV regimen were higher than in those who were treated with a DTG-based regimen, which is comparable to studies done in Zambia (Dijk et al. 2011) and Uganda (Agegnehu et al. 2020). Collectively these findings seem to lend support to the use of dolutegravir (DTG), which the WHO is currently recommending as first-line ART, and which has a higher barrier to resistance compared with NRTIs and NNRTIs regimens (McCluskey et al. 2018; WHO 2017; Gupta et al. 2018; McCluskey et al. 2018). Indeed, results of a recent study conducted in Uganda found no HIV polymorphism associated with DTG resistance, lending further support for the use of DTG (McCluskey et al. 2018).

Although other studies found a significant association between non-suppression and age at ART initiation (Bulage et al. 2017; Muri et al. 2017; Nabukeera et al. 2021). However, the current study found no significant association. These controverting findings could be explained by a high proportion of viral non-suppression in the age group (1–4 years) and (5–9 years) compared to other studies. The study found no association between TB co-infection or IPT with VL non-suppression, which was also reported in a previous study (Agegnehu et al. 2020; Negash et al. 2020). We speculate that the low percentage of participants with TB in this study may partly explain the lack of association. The hazard of non-suppression was higher in WHO clinical stages IV compared to stage III and among those who did not disclose their HIV status, but these differences were not statistically significant, in keeping with previous studies (Gupta et al. 2018; Maena et al. 2021). However, our finding is inconsistent with a previous study conducted in Uganda (Nabukeera et al. 2021). Unlike the study conducted in Uganda, only a small proportion of our clients were in WHO stage IV. The lack of association between HIV VL suppression with disclosure status points out the need to strengthen support for caregivers and promotion of child-friendly support programs.

Finally, we consider this study that focuses on HIV VL non-suppression among HIV-infected children and adolescents who are on ART to be important given the relative number of few studies conducted in this age group in Africa. The strength of this study was it was conducted meticulously using solid statistical analysis and involved a fairly big number of study participants. However, the study had the following limitations; some participants were either lost to follow-up, dead or transfer out patients, which might have caused an overestimation or underestimation VL non-suppression.

Conclusions

This study found HIV VL a high proportion of HIV VL non-suppression proportion (32.8%) among HIV-infected children and adolescents who were on ART for at least six months, in Tabora region. The overall rate of non-suppression was 1.4 per 100 PM observations and was significantly associated with poor ART adherence, NVP-, EFV-, and LPV/r-based ARV regimen, second-line ART regimen, and low baseline CD4 count at the time of ART initiation. Thus, the study supports early HIV testing and initiation of a DTG-based regimen and strong support to maintain a good level of ART adherence.

Abbreviations

AHR: Adjusted hazard ratio; AIC: Akaike information criterion; AIDS: Acquired immunodeficiency syndrome; ART: Antiretroviral therapy; BIC: Bayesian

information criterion; CD4: CD4+ T cell; CDC: Centers for Disease Control and Prevention; CI: Confidence interval; CTC: Care and treatment clinics; HIV: Human immunodeficiency virus; IAC: Intensive adherence counselling; KRRH: Kitete Regional Referral Hospital; LMIC: Low- and middle-income countries; MUHAS: Muhimbili University of Health and Allied Sciences; NACP: National AIDS Control Programme; PEPFAR: President's Emergency Plan for AIDS Relief; PLHIV: People living with HIV; THIS: Tanzania HIV impact survey; UNAIDS: United Nations Programme on HIV and AIDS; UNICEF: United Nations Children's Fund; VNS: Viral load non-suppression; VLS: Viral load suppression; WHO: World Health Organization.

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Author contributions
All authors have read and approved the manuscript and take responsibility for the integrity of the data and the accuracy of the data analysis. RDM, AKH, MIM conceptualized and designed the study; RDM collected laboratory data; RDM and AKH performed data cleaning and analysis; RDM, AKH, MIM drafted the manuscript. All authors read and approved the final manuscript.

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Availability of data and materials
Data generated during and/or analysed during the current study are available from the corresponding authors upon reasonable request.

Declarations

Ethical approval and consent to participate
Ethical approval for the study was sought from the Muhimbili University of Health and Allied Sciences (MUHAS) Institution Research Board (IRB) reference number DA.282/298/01.C/. Permission of using patients was obtained from each of the administrative levels from the regional to the district level. Data officers in the facilities removed patients' identifications including names, and phone numbers, from the dataset. Medical records were assigned a unique code, kept strictly confidential and used for research purposes only.

Consent for publication
Not applicable.

Competing interests
All authors declare that they have no commercial or other associations that may pose a conflict of interest.

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