


RESEARCH

Open Access



Determinants of nonsuppression of HIV viral load among children receiving antiretroviral therapy in the Simiyu region: a cross-sectional study

Kihulya Mageda^{1,5*} , Khamis Kulemba², Wilhelmina Olomi³, Ntuli Kapologwe^{1,5}, Leornad Katalambula¹ and Pammla Petrucka⁴

Abstract

Background Despite substantial antiretroviral therapy (ART) coverage among individuals with human immunodeficiency virus (HIV) infection in Tanzania, viral load suppression (VLS) among HIV-positive children receiving ART remains intolerably low. This study was conducted to determine factors affecting the nonsuppression of VL in children with HIV receiving ART in the Simiyu region; thus, an effective, sustainable intervention to address VL nonsuppression can be developed in the future.

Methods We conducted a cross-sectional study including children with HIV aged 2–14 years who were currently presenting to care and treatment clinics in the Simiyu region. We collected data from the children/caregivers and care and treatment center databases. We used Stata™ to perform data analysis. We used statistics, including means, standard deviations, medians, interquartile ranges (IQRs), frequencies, and percentages, to describe the data. We performed forward stepwise logistic regression, where the significance level for removal was 0.10 and that for entry was 0.05. The median age of the patients at ART initiation was 2.0 years (IQR, 1.0–5.0 years), and the mean age at HIV VL (HVL) nonsuppression was 8.8 ± 2.99 years. Of the 253 patients, 56% were female, and the mean ART duration was 64 ± 33.07 months. In multivariable analysis, independent predictors of HVL nonsuppression were older age at ART initiation (adjusted odds ratio [AOR] = 1.21; 95% confidence interval [CI] 1.012–1.443) and poor medication adherence (AOR, 0.06; 95% CI 0.004–0.867).

Conclusions This study showed that older age at ART initiation and poor medication adherence play significant roles in HVL nonsuppression. HIV/AIDS programs should have intensive interventions targeting early identification, ART initiation, and adherence intensification.

Keywords Viral load suppression, HIV-infected children, Antiretroviral therapy, Adherence

*Correspondence:

Kihulya Mageda
mageda121@gmail.com

Full list of author information is available at the end of the article



© The Author(s) 2023. **Open Access** This article is licensed under a Creative Commons Attribution 4.0 International License, which permits use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if changes were made. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit <http://creativecommons.org/licenses/by/4.0/>. The Creative Commons Public Domain Dedication waiver (<http://creativecommons.org/publicdomain/zero/1.0/>) applies to the data made available in this article, unless otherwise stated in a credit line to the data.

Background

The introduction of antiretroviral therapy (ART) and increased access to effective human immunodeficiency virus (HIV) prevention, diagnosis, treatment, and care, including opportunistic infection prevention, have heralded essential changes in the natural course of HIV infection in adults and children [1, 2]. Therefore, morbidity and mortality in adults and children have decreased [3].

To end the AIDS epidemic as a public health risk, the Joint United Nations Programme on HIV/AIDS (UNAIDS) Fast-Track approach set a target for 95% of all people living with HIV (PLHIV) to know their HIV status (diagnosed). In addition to this target, corresponding targets include the following: 95% of people with HIV infection should be started on ART, 95% of those on ART should achieve sustainable viral suppression by 2030, and there should be zero discrimination [4]. The attainment of these targets will potentially reduce new HIV infections by 95%, thus providing an opportunity to end the AIDS epidemic by 2030 [5].

Viral load suppression (VLS) is an essential parameter of ART effectiveness as a surrogate marker for disease progression [6, 7]. The aim of ART administration in children is to suppress HIV replication and halt disease progression while reducing opportunistic infections and morbidity [8, 9]. Subsequently, this approach promotes optimal growth and maximizes the health and well-being of children with HIV infection. Unfortunately, a low proportion of children with HIV in the Eastern Africa region compared with those in other countries in sub-Saharan Africa have a high risk of developing AIDS [10, 11]. In Tanzania, National AIDS Control Program data and the Tanzania HIV Impact Survey show that VLS in pediatric patients continues to be low [12–14]. Several studies have reported various factors causing VL nonsuppression, such as poor adherence, comorbidities [15–17], malnutrition [18, 19], underlying tuberculosis infection [20], and advanced disease [21].

In Tanzania, most HIV infections in children are acquired through mother-to-child transmission during pregnancy, delivery, or breastfeeding [22]. In children older than 18 months, the diagnosis of HIV infection is made through the detection of antibodies using HIV rapid tests. In infants and children under the age of 18 months, HIV infection is confirmed by HIV DNA polymerase chain reaction. HVL monitoring is performed routinely to monitor children, usually 6 months post-ART initiation. If the VL is more significant than 1000 copies/mL, the caregiver receives enhanced adherence counseling and the child is retested after 3 months [22].

Despite substantial ART coverage in PLHIV in Tanzania, VLS among HIV-positive children receiving ART

remains intolerably low at 18%, indicating that 82% of those enrolled at care and treatment centers (CTCs) receiving ART do not have VLS [12]. Despite the efforts made by the Tanzania National HIV Control Program to increase retention and adherence to care, VLS has not been effectively achieved among children [23].

Therefore, this study was designed to determine factors affecting VL nonsuppression in children with HIV infection receiving ART. The findings of this study will help us fill the knowledge gap about the factors contributing to VL nonsuppression among children with HIV infection in Tanzania.

Methods

Study design and setting

We conducted a cross-sectional analytical study in the Simiyu region. Administratively, the region comprises six districts with an estimated population of 2 million individuals. It has 218 health facilities (8 hospitals, 17 health centers, and 193 dispensaries), of which 106 provide ART services [24]. We obtained our sample from 48 of the 106 facilities. The main activity of the population in this region is agriculture, followed by livestock care. We conducted this study from October 25 to November 30, 2021.

Study population

The study population included children with HIV aged 2–14 years who were enrolled or currently receiving treatment at CTCs.

Sample size determination

We calculated the required sample size using the following formula [25]:

$$n = Z^2 P (1 - P) / \epsilon^2,$$

where n is the minimum sample size; Z is the standard average deviation of 1.96, corresponding to a 95% confidence interval (CI); P is the prevalence of VLS in children, which was 18% [26]; and ϵ indicates the degree of accuracy of the results, which was 0.05.

The calculated final sample size, with an additional 10% for incomplete data, was 253.

Sampling procedure

Multistage stratified sampling was used to select CTCs for inclusion in the study. Of the 106 health facilities offering care and treatment services (i.e., CTCs), five were hospitals, 16 were health centers, and 85 were dispensaries. All hospitals and health centers were included in the study, whereas one-third of the dispensaries were randomly selected from each district for inclusion. During the study, one health center was excluded because

two health centers were present in the same location, so random selection was performed to include one health center. A total of 48 facilities were included to represent CTCs in the Simiyu region, including 28 dispensaries, 15 health centers and five hospitals. All children with HIV infection aged between 2 and 14 years who presented to the selected health facilities and met the eligibility criteria were included in the study.

Data collection

The study was introduced to all caregivers with their children in waiting rooms, and the children were screened for inclusion criteria after receiving routine care. After obtaining written informed consent, the caregivers were interviewed using a questionnaire adapted from the National AIDS Control Program to collect basic demographic information, such as the current age and educational status of the child, the caregiver's relationship to the child, source of income, and distance from the home to the health facility. Other child clinical and demographic information, such as the child's age at ART initiation, sex, ART duration, regimen, weight, WHO clinical stage, ART adherence, and viral load, were extracted from the CTC electronic databases and exported to Excel™. The research assistants, who had medical backgrounds, were well trained in the data collection process.

Study variables and measurements

Dependent variable

The primary outcome was VL nonsuppression. VL suppression was defined as HIV-1 RNA VL of less than 1000 copies/mL. The variable was labeled as 0 = VL suppression and 1 = VL nonsuppression (HIV-1 RNA VL of greater than 1000 copies/mL).

Independent variables

The independent variables were the child's age at ART initiation, current age, sex, ART duration, regimen, weight, WHO clinical stage, and ART adherence. The independent category variables were coded such that sex was coded as "female" or "male"; regimen was coded as "first line" or "second line"; WHO stage was coded as "stage I," "stage II," "stage III," or "stage IV"; and adherence was coded as "good" or "poor." We selected the variables based on their known clinical importance through different studies.

Data analysis and presentation

We used Stata™ to analyze the obtained data. Descriptive statistics, such as means, standard deviations, medians, interquartile ranges (IQRs), frequencies, and percentages, are used to describe the data. Pearson chi-square

tests or Fisher's exact test were used to evaluate bivariate associations between sociodemographic variables and suppression status.

We used logistic regression to predict whether the VLS of a participant varied according to selected variables. We tested overall equality among variables in terms of log odds of VLS, and we compared the levels of the variables. We calculated predictive margins to show the probability of HVL nonsuppression using different variables, and a graph was drawn to visualize the results of the regression model.

We performed forward stepwise logistic regression, where the significance level for removal was 0.10 and the level for entry was 0.05. Adjusted odds ratios (AORs) and 95% CIs are presented.

The Hosmer and Lemeshow test was used to examine whether the final model adequately fit the data for the multiple logistic regression models. We performed an interaction test to examine the heterogeneity effect. We presented the final parsimonious model (i.e., the model with significant findings for predictors). The model-building procedure and guidelines for reporting regression analysis have previously been described in detail elsewhere [26].

Results

Study population characteristics

The median age of the 253 children at ART initiation was 2.0 years (IQR, 1.0–5.0 years) (Table 1), and the mean age at nonsuppression VL was 8.8 ± 2.99 years. Among the 253 children, 56% were female, and the median ART duration was 64.0 months (IQR, 37–83 months).

Most children were receiving first-line treatment regimens 99.2%; 61% had poor medication adherence; and 93% were virally suppressed (Table 1). Table 1 also shows the results of the bivariate analysis that indicate a significant variation in VLS among the medication adherence variables.

Predictors of VLS

Table 2 shows the results of multivariable analysis, older age at ART initiation (AOR, 1.21; 95% CI 1.012–1.443) was an independent predictor of VL nonsuppression, indicating that there is a 21% increase in the odds of VL nonsuppression for a 1-year increase in age at ART initiation. The final independent predictor of VLS was medication adherence (AOR, 0.06; 95% CI 0.004–0.867), indicating that children with high adherence had 94% lower odds of VL nonsuppression. The remaining factors examined as independent predictors of VL nonsuppression showed no significant effects.

Table 1 Demographic and clinical characteristics of the study population according to suppression status, N = 253

Variable	Mean (std)	Median (IQR)	Suppression	Nonsuppression	Proportion N (%)	P values
Age at ART initiation (years)		2.00 (1–5)				
Current age (years)	8.8 (2.99)					
Weight at ART initiation (kg)	24.12 (7.24)					
ART duration (months)		64.0 (37–83)				
Sex						
Female			134 (56.8)	9 (52.9)	143 (56.52)	0.758*
Male			102 (43.2)	8 (47.1)	110 (43.48)	
WHO stage ^a						
Stage I			38 (16.1)	5 (29.4)	43 (17.00)	0.577*
Stage II			43 (18.2)	3 (17.7)	46 (18.18)	
Stage III			116 (49.2)	7 (41.2)	123 (48.62)	
Stage IV			39 (16.5)	2 (11.8)	41 (16.21)	
Adherence						
Good			97 (41.1)	1 (5.9)	98 (38.74)	0.003**
Poor			139 (58.9)	16 (94.1)	155 (61.26)	
Regimen						
First-line			235 (99.6)	16 (94)	251 (99.21)	0.130**
Second-line			1 (0.4)	1 (5.9)	2(0.79)	

ART: Antiretroviral Therapy;^aWHO: World Health Organization clinical stage of HIV patients; *Pearson chi-square test; ** Fisher's exact

Table 2 Results of multivariable analysis using multiple inputs

Variable	ODR	% change	Standard error	t	P> z	95% CI (lower)	95% CI (higher)
Age at ART initiation	1.21	21	0.11	2.10	0.037	1.012	1.443
Adherence							
Good	0.06	– 94	0.08	– 2.08	0.039	0.004	0.867
Poor	1					1	1
Regimen							
First-line	0.02	– 98	0.02	– 3.52	0.001	0.003	0.183
s-line	1					1	1

Visualization by regression of predictors of VLS failure

a. Continuous variables

Figure 1 shows the relationship between the continuous independent variables and the predictive margin for the probability of HVL nonsuppression. The predictive probability of HVL nonsuppression increased as age at ART initiation increased; this relationship was significant but nonlinear (Part A). The predictive probability for VLS was also related to the age at which non VL suppression occurred. Nonsuppression trends ranged from the age of 5 years up to 14 years (Part B). Regarding ART duration, the predictive probability for VL nonsuppression decreased gradually as the ART duration increased; however, this relationship was nonlinear (Part C).

b. Categorical variables.

Figure 2 shows the relationship between the categorical independent predictor variables and the predictive margin for the probability of HVL nonsuppression. The predictive margins for the probability of VLS by WHO stage at the time of ART initiation were nonlinear, as depicted in Part A. Part B shows that the predictive margin for VL nonsuppression was higher when it changed from good adherence to poor adherence, which was linear.

In contrast, Table 3 shows the prediction of HVL nonsuppression according to WHO stage. The log odds of VL nonsuppression for stage II were not significantly different from those for stage I ($z = -0.83$, $p = 0.406$), with

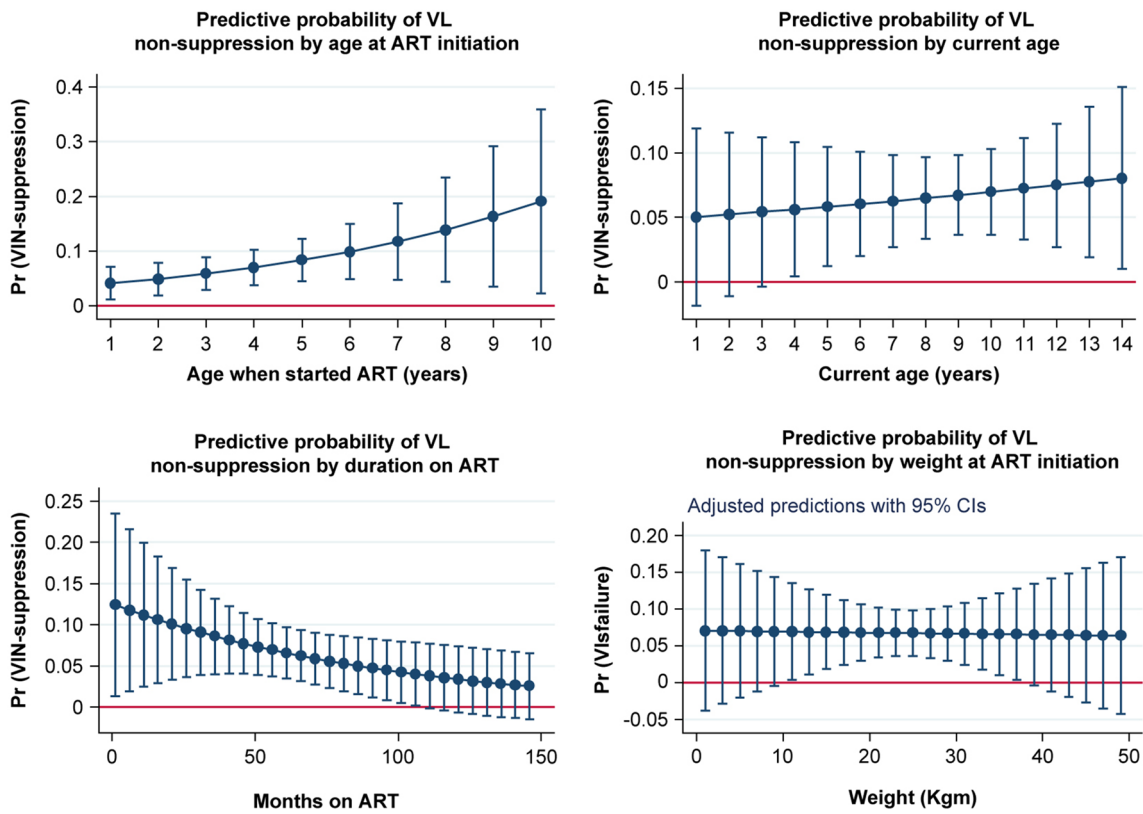


Fig. 1 Visualization of independent continuous variables for VL nonsuppression (with 95% confidence intervals)

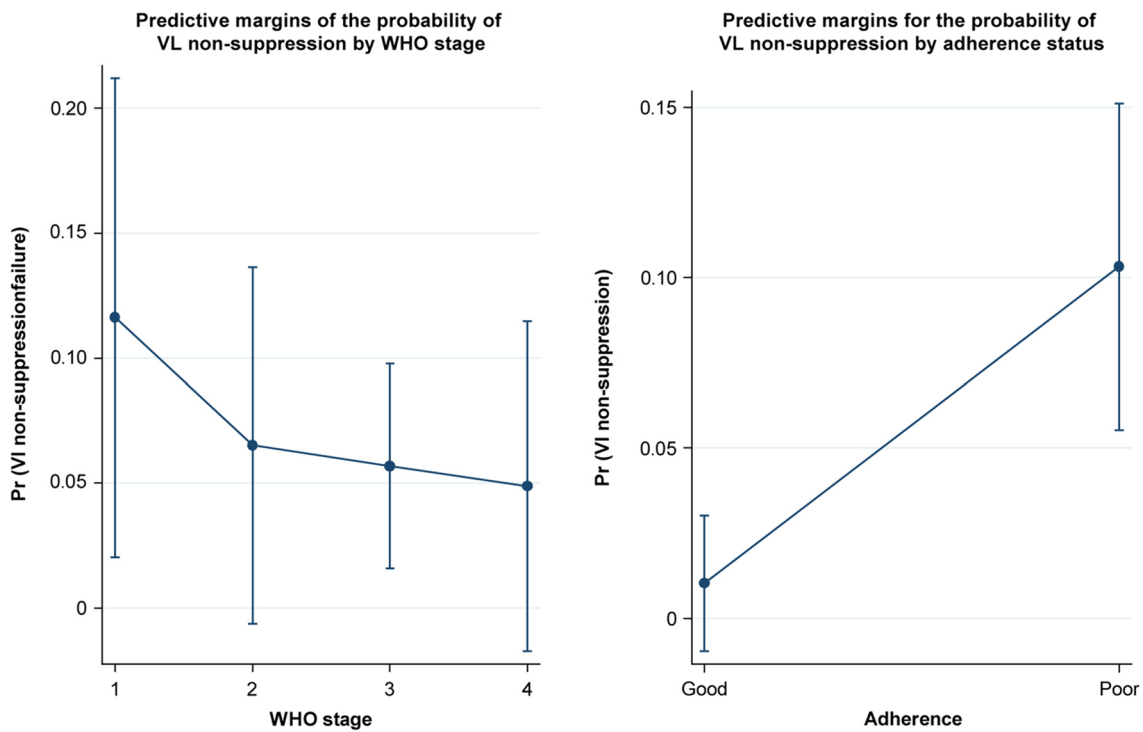


Fig. 2 Visualization of independent categorical variables predicting viral load suppression (VLS) (adjusted prediction with 95% CIs)

Table 3 Contrast among the WHO stages based on their predictive probability of HVL nonsuppression

Variable	Contrast (odds ratio)	Standard error	z	P > z	95% CI (lower)	95% CI (upper)
WHO stage						
(II vs. I)	0.53	0.41	- 0.83	0.406	0.12	2.37
(III vs. II)	0.87	0.62	- 0.20	0.839	0.21	3.50
(IV vs. III)	0.85	0.70	- 0.20	0.843	0.17	4.26

the same observed for stage III versus stage II ($z = -0.20$, $p = 0.839$) and for stage IV versus stage III ($z = -0.20$, $p = 0.843$). Thus, the WHO stage at ART initiation was not associated with VLS.

Discussion

In response to the HIV epidemic, Tanzania is implementing preventive care, treatment, and support interventions to achieve the global targets of 95/95/95 by 2030 [22]. In both rural and urban settings, HIV testing and antiretroviral drugs are freely available to people with HIV. HIV VL monitoring is available and performed routinely to monitor all clients receiving ART, usually 6 months post-ART initiation.

This study revealed valuable findings regarding the factors affecting VLS in children with HIV infection who were receiving ART. In particular, approximately 17% of the interviewed participants had VL nonsuppression. Factors associated with VL nonsuppression include older age at ART initiation and poor medication adherence.

This study revealed that older age at ART initiation was significantly associated with HVL nonsuppression. Thus, HVL nonsuppression increases as age increases. The findings indicate that starting ART early, when viral replication is still low, hastens the response to therapy when compared to starting ART later, when HIV is in the advanced stage. These findings contradict each other as children get older because their adherence becomes poor and psychosocial problems become prominent after starting school. Jiamsakul et al. [10] reported that children who initiated ART at a younger age were more likely to achieve VLS. Moreover, Tagarro et al. [27] confirmed the relevance of early ART initiation as a key factor leading to smaller viral reservoir size. Children who started ART earlier were less likely to experience viral rebounds than those who started ART later. The age at ART initiation presented a linear association with VLS, which was demonstrated by Foster et al. [28]. These findings provide additional support for the early initiation of ART in HIV-infected infants [29]. Our results indicate that early ART initiation in children with HIV reduces the risk of VLS failure; thus, interventions should focus on managing

HIV in children in this age group. This result suggests that early initiation of therapy influences key virological and immunological parameters that could have significant effects on long-term health [30].

This study revealed the relationship between the ages at which VLS fails. It shows that VLS failure starts at the age of 5 years; however, this was not statistically significant and was removed from the final model. At the age of 7 years, children become partially independent because they have started school and their HIV status has been disclosed to them. Mu et al. reported on the relationship between age and VLS in children receiving ART [31]; children aged 6 years and older are more likely than younger children to have HVL nonsuppression. Older age, notably an age of more than 10 years, was associated with an increased risk of HVL nonsuppression [32]. This was potentially due to treatment nonadherence, as ART was started during a developmentally sensitive period of early life, and continuous education therapy and interventions are essential to improve adherence [33]. Our visualization indicates that age is an essential factor to consider during the care of children, particularly regarding screening and frequent follow-up, which could improve a child's adherence to treatment.

This study revealed the relationship between ART duration and VLS. It showed that HVL nonsuppression decreased progressively as the ART duration decreased. Although this finding was not statistically significant and was removed from the final model, it could be clinically significant in the care and treatment of children. These results contradict other findings demonstrating that children who had been on ART for a longer duration (>5 years) were more likely to achieve VLS [34], and a higher proportion of children had achieved VLS after 4 years of treatment [35]. Our visualization depicts that more intensive intervention is needed during the early months of ART initiation when nonadherence or VLS failure is detected or suspected.

This study showed that some children were switched from first-line regimens to second-line regimens due to high VL. These findings suggest the probability of early resistance of the first-line regimen to ART. Moreover,

they highlighted the likelihood of resistance secondary to adherence status. Henerico et al. (2022) proved that a single high VL result (greater than 1000 copies/mL) at any point during ART is associated with a high probability of drug resistance, thus serving as a predictor of virological failure [36]. Desmond et al. [37] reported that the most common reason for switching from a first-line regimen to a second-line regimen was nonadherence, as observed in older children, who have longer periods since ART initiation. In other studies, the ART regimen type was demonstrated to be the only significant factor associated with VLS [38], whereas Johnston et al. [39] reported that nonadherence significantly contributes to regimen switching. This study did not have adequate data to demonstrate the existence of this phenomenon; thus, further studies are needed to identify the determinants of regimen changes.

This study provided evidence that medication adherence was significantly associated with VLS in this population. Children who had poor adherence were more likely to experience HVL nonsuppression than those with exemplary dedication. This shows that poor medication adherence enables the virus to replicate faster, leading to the failure of the drugs to suppress the virus. Additionally, poor adherence increases the risk of developing drug resistance and the occurrence of opportunistic infections; thus, the virus replicates more frequently and faster. Bitwale et al. showed that poor ART adherence in Tanzania was associated with virological treatment failure [40]. Similarly, another study in Tanzania showed that poor ART adherence was associated with childhood treatment failure [41]. Our findings were similar to those of other studies outside Tanzania demonstrating that nonadherence to ART increased the odds of HVL nonsuppression by fivefold [34]. Better adherence reduces the risk of VL nonsuppression [42]. These findings indicate that adherence to treatment among children receiving ART is an essential indicator of better VLS and improves well-being. Thus, HIV programs should incorporate interventions to mitigate the risk of poor adherence. However, we also observed that a substantial proportion of children who were nonadherent showed VL suppression at 6 months. This finding may be explained by the potential of most ART regimens to suppress VL even with some missed doses. Additionally, the categorization of adherence status was dichotomized where children who had missed two doses were still considered nonadherent. The categorization may have limited the ability to exhibit the linearity between the number of missed doses and the level of viral nonsuppression.

This study had several limitations. Throughout the region, the CD4 machine was not working, and the majority of children were not tested for CD4 cell count at ART initiation. Thus, there could be bias in our

conclusions because these factors have significant clinical importance. The number of participants who switched from first-line regimens to second-line regimens was small. Furthermore, some children arrived with caregivers who were not their parents; therefore, they could not recall when the child became infected with HIV, so our data lack a model of participant infection. Furthermore, a cross-sectional study design was adopted in this study, which cannot show a causal relationship; thus, further analytical studies are needed, such as cohort and experimental studies. Moreover, our cross-sectional design did not include children who died or were lost to follow-up. Because these children were more likely to have experienced virologic failure, the results were biased toward better viral suppression by (naturally) excluding them.

Despite these limitations, the study's strength was that we used advanced regression to visualize the essential factors when managing children with HIV infection.

Conclusions

In this study, older age at ART initiation and poor medication adherence played a significant role in VLS. We recommend that interventions targeting early ART initiation for children and intensified adherence should be strengthened. Thus, there is a need to identify a sustainable intervention that promotes adherence to ART and addresses low VLS among children with HIV infection in Tanzania.

Abbreviations

AOR	Adjusted odds ratio
ART	Antiretroviral therapy
CTC	Care and treatment center
HIV	Human immunodeficiency virus
IQRs	Interquartile ranges
PLHIV	People living with HIV
VL	Viral load
VLS	Viral load suppression

Acknowledgements

The authors acknowledge the Simiyu Regional Health Management Team for their support.

Author contributions

The authors confirmed contribution to the paper: Study conception, design, data analysis and presentation: KM, PP, LK, and WO; data collection and manuscript drafting and preparations: KK, KM; manuscript review: PP, LK, and NK. LK and PP approved the final version of the manuscript. All authors read and approved the final manuscript.

Funding

This research received no specific funding from individuals or organizations.

Availability of data and materials

Supplementary data are available in the journal and can be accessed upon request.

Declarations

Ethics approval and consent to participate

The protocol for this study was reviewed and approved on October 18, 2021, by the Institutional Ethics Clearance Board of the University of Dodoma (reference number MA:84/261/02/"A"). Informed consent for participation was obtained from the children's caregivers, and we ensured that consent forms were signed before participation in the study. Throughout the study, we adhered to the confidentiality principle that no personal identifiers be included in the data, and the data were not accessible to any person who was not a part of the study team.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

Author details

¹School of Nursing and Public Health, University of Dodoma, PO Box 395, Dodoma, Tanzania. ²Department of Health, Simiyu Regional Commissioners' Office, Bariadi, Tanzania. ³National Institute for Medical Research Mbeya, Mbeya, Tanzania. ⁴University of Saskatchewan, Saskatoon, Canada. ⁵President's Office—Regional Administration and Local Government, PO Box 1923, Dodoma, Tanzania.

Received: 23 November 2022 Accepted: 3 April 2023

Published online: 13 April 2023

References

- World Health Organization. HIV/AIDS fact sheet. 2020. [cited 2021 April]. <https://www.who.int/health-topics/hiv-aids>. Accessed 15 June 2021.
- Zanchetta M, Anselmi A, Vendrame D, Rampon O, Giaquinto C, Mazza A, et al. Early therapy in HIV-1-infected children: effect on HIV-1 dynamics and HIV-1-specific immune response. *Antivir Ther*. 2008;13:47–55.
- Kovacs A, Montepiedra G, Carey V, Pahwa S, Weinberg A, Frenkel L, et al. Immune reconstitution after receiving highly active antiretroviral therapy in children with advanced or progressive HIV disease and complete or partial viral load response. *J Infect Dis*. 2005;192:296–302.
- United Nations Program on HIV/AIDS (UNAIDS). 2019. Start free stay free AIDS [cited 2020 February 30]. https://www.unaids.org/sites/default/files/media_asset/20190722_UNAIDS_SFSFAF_2019_en.pdf. Free Press. Accessed 20 Nov 2020.
- United Nations Program on HIV/AIDS. 2012. Promising practices in community engagement for the elimination of new HIV infections among children by 2015 and keeping their mothers alive; 2015. UNAIDS Case Study. https://www.unaids.org/sites/default/files/media_asset/20120628_JC2281_PromisingPracticesCommunityEngagements_en_0.pdf. Accessed 15 Nov 2021.
- Ali JH, Yirtaw TG. Time to viral load suppression and its associated factors in cohort of patients taking antiretroviral treatment in East Shewa zone, Oromiya, Ethiopia, 2018. *BMC Infect Dis*. 2019;19:1084.
- World Health Organization. Consolidated Guidelines on the Use of Antiretroviral Drugs for Treating and Preventing HIV Infection Recommendations for a Public Health Approach. 2016. 2nd ed [cited 2019 September 21]. <https://www.who.int/hiv/pub/arv/arv-2016/en/>. Accessed 21 Sep 2019.
- Abrams EJ, Woldeesenbet S, Soares Silva J, Coovadia A, Black V, Technau KG, et al. Despite access to antiretrovirals for prevention and treatment, high mortality rates persist among HIV-infected infants and young children. *Pediatr Infect Dis J*. 2017;36:595–601.
- Anigilaje EA, Aderibigbe SA. Mortality in a cohort of HIV-infected children: a 12-month outcome of antiretroviral therapy in Makurdi, Nigeria. *Adv Med*. 2018;2018:6409134.
- Jiamsakul A, Kariminia A, Althoff KN, Cesar C, Cortes CP, Davies MA, et al. HIV viral load suppression in adults and children receiving antiretroviral therapy—results from the leDEA collaboration. *J Acquir Immune Defic Syndr*. 2017;76:319–29.
- Teasdale CA, Sogaula N, Yuengling KA, Wang C, Mutiti A, Arpadi S, et al. HIV viral suppression and longevity among a cohort of children initiating antiretroviral therapy in Eastern Cape, South Africa. *J Int AIDS Soc*. 2018;21:e25168.
- President's Emergency Plan for AIDS Relief [internet]. Tanzania country operational plan COP2019 strategic direction summary. 2019. [cited 2019 May 10]. https://www.state.gov/wp-content/uploads/2019/09/Tanzania_COP19-Strategic-directional-Summary_public.pdf. Accessed 5 Nov 2020.
- Tanzania Commission for AIDS. (TACAIDS)& Zanzibar AIDS commission (ZAC). Tanzania HIV Impact Survey (THIS). 2016–2017 [final report]. Dar es Salaam, Tanzania. ; 2018 [cited 2019 September 21]. www.nbs.go.tz/index.php/en/census-surveys/health-statistics/hiv-and-malaria-survey/382-the-tanzania-hiv-impact-survey-2016-2017-this-final-report. Accessed 21 Sep 2019.
- President's Emergency Plan for AIDS Relief (PEPFAR). Tanzania country operational plan COP2017 strategic direction summary. 2017. [cited 2017 March 2]. <https://tz.usembassy.gov/wp-content/uploads/sites/258/2017/07/TZ-COP-2017-SDS-FINAL-Update-29June2017.pdf>. Accessed 5 Nov 2020.
- Barnabas RV, Webb EL, Weiss HA, Wasserheit JN. The role of co-infections in HIV epidemic trajectory and positive prevention: a systematic review and meta-analysis. *AIDS*. 2011;25:1559–73.
- Bulage L, Ssewanyana I, Nankabirwa V, Nsubuga F, Kihembo C, Pande G, et al. Factors associated with virological non-suppression among HIV-positive patients on antiretroviral therapy in Uganda, August 2014–July 2015. *BMC Infect Dis*. 2017;17:326.
- Martelli G, Antonucci R, Mukurasi A, Zepherine H, Nöstlinger C. Adherence to antiretroviral treatment among children and adolescents in Tanzania: comparison between pill count and viral load outcomes in a rural context of Mwanza region. *PLoS ONE*. 2019;14:e0214014.
- Bartelink IH, Savic RM, Dorsey G, Ruel T, Gingrich D, Scherpier HJ, et al. The effect of malnutrition on the pharmacokinetics and virologic outcomes of lopinavir, efavirenz and nevirapine in food insecure HIV-infected children in Tororo, Uganda. *Pediatr Infect Dis J*. 2015;34:e63–70.
- Muenchhoff M, Healy M, Singh R, Roider J, Groll A, Kindra C, et al. Malnutrition in HIV-infected children is an indicator of severe disease with an impaired response to antiretroviral therapy. *AIDS Res Hum Retrovir*. 2018;34:46–55.
- Gupta RK, Lucas SB, Fielding KL, Lawn SD. Prevalence of tuberculosis in post-mortem studies of HIV-infected adults and children in resource-limited settings: a systematic review and meta-analysis. *AIDS (Lond Engl)*. 2015;29:1987–2002.
- Anigilajé EA, Aderibigbe SA, Adeoti AO, Nweke NO. Tuberculosis, before and after antiretroviral therapy among HIV-infected children in Nigeria: what are the risk factors? *PLoS ONE*. 2016;11:e0156177.
- The National Guidelines for the Management Of HIV and AIDS. The United Republic of Tanzania Ministry of Health and Social welfare 7th ed. 2019. <https://nacp.go.tz/download/national-guidelines-for-the-management-of-hiv-and-aids>. Accessed 15 Apr 2021.
- The Second National HIV and AIDS Health Sector Research and Evaluation Agenda. The United Republic of Tanzania Ministry of Health and Social welfare, (2019–2024). 2020.
- District health information system (DHIS. 2) [internet] [cited December 2021]. <https://dhis.moh.go.tz/dhis-web-commons/security/login.action>. Accessed 21 Mar 2021.
- Cochran WG. Sampling techniques. 3rd ed. Hoboken: Wiley; 1977.
- Hosmer DW, Lemshow S. In: Applied logistic regression. Second Edition. A <https://onlinelibrary.wiley.com/doi/book/10.1002/9781118548387>. Accessed 20 October 2021.
- Tagarro A, Chan M, Zangari P, Ferns B, Foster C, De Rossi A, et al. Early and highly suppressive antiretroviral therapy are main factors associated with low viral reservoir in European perinatally HIV-infected children. *J Acquir Immune Defic Syndr*. 2018;79:269–76.
- Foster C, Dominguez-Rodríguez S, Tagarro A, Gkouleli T, Heaney J, Waters S, et al. The CARMA study: early infant antiretroviral therapy-timing impacts on total HIV-1 DNA quantitation 12 years later. *J Pediatr Infect Dis Soc*. 2021;10:295–301.
- Shiau S, Strehlau R, Technau KG, Patel F, Arpadi SM, Coovadia A, et al. Early age at the start of antiretroviral therapy associated with better

- virologic control after initial suppression in HIV-infected infants. *AIDS*. 2017;31:355–64.
30. Chan. Predictors of faster virological suppression in early treated infants with perinatal HIV from Europe and Thailand. *AIDS (Lond Engl)*. 2019;33:1155–65.
 31. Mu W, Bartlett AW, Bunupuradah T, Chokephaibulkit K, Kumarasamy N, Ly PS, et al. Early and late virologic failure after virologic suppression in HIV-infected asian children and adolescents. *J Acquir Immune Defic Syndr*. 2019;80:308–15.
 32. Duong T, Judd A, Collins IJ, Doerholt K, Lyall H, Foster C, et al. Long-term virological outcome in children on antiretroviral therapy in the UK and Ireland. *AIDS*. 2014;28:2395–405.
 33. Prendergast AJ, Penazzato M, Cotton M, Musoke P, Mulenga V, Abrams EJ, Gibb DM. Treatment of young children with HIV infection: using evidence to inform policymakers. *PLOS Med*. 2012;9:e1001273.
 34. Gaitho D, Kemunto D, Kinoti FK, Lawrence M, Catherine N. Determinants of viral non-suppression among children in an HIV program in Kenya: a cross-sectional study. *Sex Transm Infect*. 2019;95:A128–9.
 35. Fraaij PL, Verweel G, van Rossum AM, van Lochem EG, Schutten M, Weemaes CM, et al. Sustained viral suppression and immune recovery in HIV type 1-infected children after four years of highly active antiretroviral therapy. *Clin Infect Dis*. 2005;40:604–8.
 36. Henerico S, Mikasi SG, Kalluvya SE, Brauner JM, Abdul S, Lyimo E, et al. Prevalence and patterns of HIV drug resistance in patients with suspected virological failure in North-Western Tanzania. *J Antimicrob Chemother*. 2022;77:483–91.
 37. Desmonde S, Eboua FT, Malateste K, Dicko F, Ekouévi DK, Ngbeché S, et al. Determinants of the durability of first-line antiretroviral therapy regimen and time from first-line failure to second-line antiretroviral therapy initiation. *AIDS (Lond Engl)*. 2015;29:1527–36.
 38. Chouraya C, Ashburn K, Khumalo P, Mpango L, Mthethwa N, Machekano R, et al. Association of antiretroviral drug regimen with viral suppression in HIV-positive children on antiretroviral therapy in ESwatini. *Pediatr Infect Dis J*. 2019;38:835–9.
 39. Johnston V, Cohen K, Wiesner L, Morris L, Ledwaba J, Fielding KL, et al. Viral suppression following switch to second-line antiretroviral therapy: associations with nucleoside reverse transcriptase inhibitor resistance and subtherapeutic drug concentrations prior to switch. *J Infect Dis*. 2014;209:711–20.
 40. Bienczak A, Denti P, Cook A, Wiesner L, Mulenga V, Kityo C, et al. Determinants of virological outcome and adverse events in african children treated with pediatric nevirapine fixed-dose-combination tablets. *AIDS (Lond Engl)*. 2017;31:905–15.
 41. Bitwale NZ, Mnzava DP, Kimaro FD, Jacob T, Mpondo BCT, Jumanne S. Prevalence and factors associated with virological treatment failure among children and adolescents on antiretroviral therapy attending HIV/AIDS care and treatment clinics in Dodoma Municipality, Central Tanzania. *J Pediatr Infect Dis Soc*. 2021;10:131–40.
 42. Gelaw B, Dessalegn L, Alem E, Tekalign T, Lankirew T, Eshetu K, et al. Prevalence and associated factors of treatment failure among children on ART in Ethiopia: a systematic review and meta-analysis. *PLoS ONE*. 2022;17:e0261611.

Publisher's Note

Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Ready to submit your research? Choose BMC and benefit from:

- fast, convenient online submission
- thorough peer review by experienced researchers in your field
- rapid publication on acceptance
- support for research data, including large and complex data types
- gold Open Access which fosters wider collaboration and increased citations
- maximum visibility for your research: over 100M website views per year

At BMC, research is always in progress.

Learn more biomedcentral.com/submissions

