

HIV virological non-suppression and its associated factors amongst children on antiretroviral therapy at a major paediatric treatment centre in Southern Ghana: a cross-sectional study

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Abstract

Background

Children with human immunodeficiency virus (HIV) infection require lifelong effective Antiretroviral Therapy (ART). The aim of ART in HIV-infected persons is sustained viral suppression. There is limited information on virological non-suppression or failure and its associated factors in children in resource limited countries, particularly Ghana.

Methods

A cross-sectional study of 250 children aged 8 months to 15 years who had been on ART for at least 6 months attending the Paediatric HIV clinic at Korle Bu Teaching hospital in Ghana was performed. Socio-demographic, clinical, laboratory and ART Adherence related data were collected using questionnaires as well as medical records. Blood samples were obtained for viral load and CD4⁺ count determination. Viral load levels > 1000 copies/ml on ART was considered virological non-suppression. Logistic regression was used to identify factors associated with virological non-suppression.

Results

The mean (\pm SD) age of the study participants was 11.4 ± 2.4 years and the proportion of males was 53.2%. Of the 250 study participants, 96 (38.4%) had virological non-suppression. After adjustment for significant variables, the factors associated with non-suppressed viral load were female gender (AOR 2.51 [95% CI 1.04–6.07], $p = 0.041$), having a previous history of treatment of tuberculosis (AOR 4.95 [95% CI 1.58–15.5], $p = 0.006$), severe CD4 immune suppression status (CD4% < 15% / CD4⁺ count < 200 cells/mm³) at study recruitment (AOR 24.93 [95% CI 4.92-126.31], $p < 0.001$) and being on a Nevirapine based regimen (AOR 7.93 [95% CI 1.58–1.15], $p = 0.005$).

Conclusion

The prevalence of virological non-suppression was high. Virological non-suppression was associated with a previous history of TB treatment, female gender, severe CD4 immune suppression status (CD4% <15% / CD4⁺ count < 200 cells/mm³), at study recruitment and being on a Nevirapine based regimen. Early initiation of ART and phasing out Nevirapine based regimen might improve viral load suppression in children. In addition, children with a history of TB may need focused measures to maximize virological suppression.

Background

Human immunodeficiency virus (HIV) infection continues to be one of the most important infectious diseases worldwide.^{1,2} Antiretroviral therapy (ART) is an important component of the overall management plan for HIV/AIDS. The primary goal of ART is to suppress viral replication, which ultimately results in restoration of the immune system, reduction of the onward transmission of the HIV virus and a general improvement in the quality of life of people infected with HIV.^{3,4} In resource-limited settings, HIV viral load (HIV VL) monitoring is recommended by the WHO (World Health Organization) as a gold standard for monitoring treatment effectiveness

in 2013,⁵ and Ghana adopted these guidelines in 2016. According to Ghana's National Aids Control Program (NACP) guidelines, viral load testing is recommended 6 months after initiating ART and thereafter annually for people who have achieved virological suppression.⁶ However people with HIV VL levels > 1000 copies/ml undergo intensified adherence support after which the viral load is repeated three months later in order to differentiate poor adherence from treatment failure.⁶

Virological non-suppression could be due to poor adherence to ART, resistance to ART (transmitted or acquired) or pharmacokinetic issues (poor absorption, under-dosing and drug interactions).^{7,8} Adherence-related factors are most often caused by the patient.^{7,8} ART regimen-related factors could result in the development of resistance.^{9,10}

A wide range of factors are associated with virological non-suppression and these include socio-demographic factors such as younger age (less than three years),¹¹ male gender,^{12,13} WHO advanced HIV stage,^{14,15} co-infection with tuberculosis (TB),^{16,17} nevirapine (NVP) based therapy,^{18,19} and poor adherence to treatment.^{20,21} A principle cause for virological non-suppression is non-adherence.^{21,22} The paediatric population are more likely to have challenges with adherence to ART^{23,24} because drug formulations for paediatric patients are often less tolerable, and require dose adjustment according to the weight as the child grows.^{23,24} There are also specific challenges with the social context, such as a lack of consistent caregiver in younger children and disclosure issues, which pose a challenge to consistent adherence.^{23,24} These peculiar issues to children and adolescents can result in virological non-suppression, without necessarily leading to the development of drug resistance.⁸

High rates of virological non-suppression suggests a higher risk of developing resistance and is common in children in Low-and middle-income countries. (LMICs)⁸, and this has implications for the spread of resistant HIV variants. Identifying patients with virological non-suppression is thus important for prompt detection of treatment failures and in identifying the characteristics of the population that might benefit from interventions such as intensified adherence counseling and increased frequency of follow up.³¹ This would in turn prevent the development of drug resistance in the population at risk. The aim of this study was therefore to determine the prevalence of virological non-suppression and its associated factors among children living with HIV (CLWH) attending a Paediatric HIV clinic at Teaching Hospital in Ghana. This knowledge would help to target interventions for improving virological suppression that will ultimately lead to improvement in clinical care.

Methods

Study design and setting

This study used a cross-sectional design to recruit paediatric HIV positive patients attending the outpatient clinic from October 2017 to July 2018 at the Korle Bu Teaching Hospital (KBTH), Accra, Ghana. KBTH has 2500 beds and is currently the largest hospital in West Africa and the third largest on the African continent.²⁵ The hospital is the main tertiary referral centre in Accra and serves the majority of the southern half of Ghana. The Paediatric HIV clinic at KBTH has been providing comprehensive HIV/AIDS care and management services since 2004. Patients are referred from primary and secondary health facilities as well as from other departments within the hospital. An average of 40 patients are seen per clinic day. The National AIDS Control Program (NACP) provides ART medication free of charge. HIV VL and CD4⁺ counts are also paid for by the program. The clinic uses national

treatment guidelines that are in line with current WHO recommendations for ART in Ghana.²⁶ Treatment is initiated for all patients irrespective of the CD4⁺ count. ART available and in use in various combinations at the clinic at the time of the study were zidovudine (AZT), lamivudine (3TC), abacvir (ABC), efavirenz (EFV), nevirapine (NVP), tenofovir (TDF), and ritonavir boosted Lopinavir (LPV/r).

Study participants

Study participants were Children living with HIV (CLHV) aged between 8 months and 15 years and who had been on ART for at least 6 months for whom caregivers/study participants had given informed written consent to participate in the study were enrolled. Children who had been transferred from referral points and did not have their previous notes available and children with HIV-2 mono infection were excluded from the study. There are currently no Food and Drug FDA-approved assays for quantification of HIV-2 RNA⁷¹ and hence the exclusion of children with HIV-2 mono infection. Voluntary informed consent was obtained from parents and guardians of study participants and assent from children aged 10-15 years. Before seeking informed consent/assent, study participants were screened to determine whether they were eligible or not. A questionnaire was administered to study participants and caregivers. Information was also collected retrospectively from their medical records.

Sample size determination

The Cochran's sample size formula²⁷ was used to calculate the sample size to determine the prevalence of non-suppressed viremia. A minimum sample size of 250 study participants was determined using confidence level of 95% and an error margin of 5%. Consecutive cases of HIV children who met the eligibility criteria were enrolled into the study until the sample size was reached.

Data Collection

Participants had their drug doses checked for appropriateness of their current drug regimen. The dosage, (frequency and dose/kg or m²) was cross checked with the recommended dosage and appropriateness was documented as 'yes' or 'no.' ART Adherence was assessed by a pharmacist on the day of recruitment using the pill count.

Pill count (the number of pills taken) was calculated based on the number of unused pills that the care giver brought back when refilling their ART medication on the day of study recruitment.¹⁵⁵ Total refill was the expected number of pills to have been taken since the last visit.

Pill count was callulated as: **see equation in the supplementary files.**

Laboratory analysis

Laboratory investigations done on the day of recruitment were CD4⁺ count and HIV VL. CD4⁺ absolute cell count and cell percentage were quantified by a dual-platform flow cytometry technology using a FACS Count system (Becton-Dickinson, Franklin Lakes, NJ, USA) according to manufacturer's instructions at the Fevers Unit Laboratory of KBTH. The HIV RNA VL testing was performed at the Central Laboratory of KBTH using the COBAS ® AMPLICOR Monitor test (Roche Diagnostic Systems, Branchburg, NJ, USA), with a a lower limit of detection of 20 copies/ml. The laboratory at the Fevers unit and the Central Lab KBTH are certified by the South African Public

Health Reference Laboratory and participates in an external quality assurance testing programme by the South African Public Health Reference Laboratory.

Operational definitions

In accordance with WHO guidelines, study participants were categorized as having virological non-suppression if the HIV VL level was > 1000 copies/ml on the day of recruitment, after at least 6 months of using ART. Drug Adherence was determined by caregivers report and categorized according to WHO guidelines as follows: Good \geq 95%; Fair: 85-94%; Poor < 85%.²⁸

Statistical analysis

The dependent variable was virological non-suppression (VL > 1000 copies/ml). The independent variables were the sociodemographic factors, clinical factors and ART Adherence factors. Pearson's chi-square test of association was used to determine strength of association between the independent categorical variables and the outcome variable (virological non-suppression). The logistic regression model was used in determining the factors influencing HIV VL suppression among study participants with statistical significance set at $p < 0.05$. The crude odds ratio (OR) and adjusted odds ratio (AOR) were determined and OR and their respective 95% confidence intervals were calculated.

Ethical considerations

Ethical approval (KBTH-IRB/ 00060/2017) was obtained from the Institutional Review Board of Korle Bu Teaching Hospital, Accra, Ghana. Informed consent was obtained from parents or legal guardians for each minor participant prior to enrolment to participate in the study.

Results

Baseline characteristics

The baseline characteristics of all 250 patients are shown in Table 1. The mean duration on ART was 64 months \pm 3.0 months. More than half 133 (53.2%) of the study participants were males. Majority of the study participants 148 (59.2%) were within the age range of 10 to 15 years. Overall, the mothers of 157 (62.8%) participants were HIV positive while 93 (37.2%) of mothers had unknown HIV status. The fathers of 62 (24.8%) study participants were HIV positive whilst 105 (42.0%) were HIV negative and 83 (33.2%) had unknown HIV status. Primary caregivers who were mothers were 115 (46.0%), fathers were 25 (10.0%) and 110 (44%) were guardians (grandmother, grandfather, aunt, uncle, foster caregiver). The unknown status included parents who were dead. The educational and occupation of parents is described in Table 1.

Clinical and laboratory details of study participants

A significant number of study participants 97 (38.8%) were in WHO clinical stage one at initiation of ART. Of all participants, 71 (28.4%) had a history of previous TB treatment.

Baseline CD4⁺ count and VL of study participants

Overall, of the 225 study participants that had records for their Baseline CD4⁺ counts, 35 (15.6%) had severe CD4 immune suppression status (CD4% <15% / CD4⁺ count < 200 cells/mm³), 25 (11.1%) had advanced CD4 immune suppression status (CD4 %: 15-19% / CD4 count: 200-349 cells/mm³), 18 (8%) had mild CD4 immune status (CD4 %: 20-25% / CD4⁺ count: 350-499 cells/mm³) with the majority of study participants 147 (65.3%) having normal CD4⁺ status (CD4 % >25% / CD4 count: > 500 cells/mm³).³ Out of the 250 study participants, only 74 (30%) had baseline VL documented. Of the 74 study participants that had records of baseline VL, a significant number 30 (40.5%), had baseline VL < 10, 000 copies/ml, 22 (29.7%) had VL levels between (10, 000 and 99,999), 12 (16.2%) have VL levels between (100,000 and 4999,999 and 10 (13.5%) have viral load levels ≥ 5000,000.

CD4⁺ count at study recruitment

The CD4⁺ results for 20 of the study participants were not available because of technical issues that occurred with their blood samples at the laboratory. Of the 230 that had CD4⁺ results on the day of study recruitment, 10 (4.3%) were children less than 5 years and 220 (95.7%) were children between 5 and 15 years of age. For the overall CD4⁺ immune suppression status, 24 (10.4%) had severe immune suppression status, (CD4% <15% / CD4 count < 200 cells/mm³), 18 (7.8%) had advanced immune suppression status (CD4%: 15-19% / CD4⁺ count: 200-349 cells/mm³), 23 (10%) had mild immune suppression status (CD4 %: 20-25% / CD4 count: 350-499 cells/mm³) and 165 (71.7%) had normal CD4⁺ immune status (CD4 %: >25% / CD4⁺ count: > 500 cells/mm³).³

Proportion of patients with virological non-suppression

At study enrolment, 96 (38.4%) of the 250 study participants had virological non-suppression (VL > 1000 copies/mls). Study participants with low-level viraemia (VL level 20-1000 copies/ml) were 58 (23.2%) and those with VL levels < 20 copies/ml were 96 (38.4%). For virological non-suppression within the various age groups, 14 (46.7%) were within the age group (< 5 years), 28 (38.9%) were within the age group (5-9 years) and 54 (36.5%) were within the age group (10 -15 years).

Factors associated with virological non-suppression

Bivariate analysis of factors associated with virological non-suppression are shown in Table 1. Females were more likely to have virological non-suppression in comparison to males (54.2% vs 32.2%, p = 0.035). The overall CD4⁺ immune suppression status of the subject at study recruitment showed a significant association with the subjects VL. (Fischer's exact (Φ, p < 0.001). The adherence rate of subject measured by pill count percentage showed a significant association with the subjects VL ($\chi^2= 7.99$, p =0.018).

There were no significant differences for the following variables: age of subject, primary caregiver's relationship to subject, educational status of father, educational status of mother, occupational status of father, occupational status of mother, history of previous TB treatment, WHO stage at initiation of ART, baseline VL and baseline CD4⁺ count values (overall), duration on ART, current ART regimen and person responsible for child's medication (Table 1).

Factors associated with virological non-suppression in multivariate analysis

In multivariate analysis of patients, females were 2.5 times more likely to have virological non-suppression when compared with male study participants (AOR 2.51 [95% CI 1.04-6.07], $p = 0.041$). Additionally, study participants with severe CD4⁺ immune suppression status at study recruitment were 9 times more likely to have virological non-suppression when compared to children with normal CD4⁺ / no immune suppression in multivariate analysis (AOR 24.93 [95% CI 4.92-126.31], $p < 0.001$). Participants with a prior history of TB treatment were 4.95 times more likely to have virological non-suppression as compared to participants without a prior history of TB treatment (AOR 4.95 [95% CI 1.58-15.5], $p < 0.006$). Participants with a NVP based regimen was 7.93 times more likely to be associated with virological non-suppression (AOR 7.93 [95% CI 1.58-15.5], $p = 0.005$). Multivariate analysis of adherence pill count did not yield any significant results (Table 2).

Table 2: Univariate and multivariate analysis of factors associated with virological non suppression in CLWH on ART for a at least 6 months (N= 250)

Factor	Univariate analysis		Multivariate analysis		AOR (95% CI)	P value
	UOR	(95% CI)	P value			
1. Sex of child	0.004*		0.041*			
Male	ref					
Female	2.52 4.67	1.35 –	2.51 – 6.07	1.04		
2. Age category	0.342				0.138	
<5 years	1.72 5.24	0.57 –	2.18 – 20.89	0.23		
5 to <10 years	1.57 3.17	0.78 –	2.84 – 8.05	1.01		
10 to 15 years	ref		ref			
3. CD4⁺ Immune suppression status at study recruitment			<0.001*			<0.001*
Severe	9.03 26.51	3.08 –			24.93 126.31	4.92–
Advanced	7.97 31.31	2.03 –	9.2 – 66.48	1.27		
Mild	3.65 9.9	1.35 –	3.75 – 15.4	0.91		
None	ref		ref			
4. TB treatment in the past	0.122				0.006*	
No	ref		ref			
Yes	1.67 3.18	0.87 –	4.95 – 15.5	1.58		
5. Current Drug	0.231		0.005*			
Efavirenz based	ref		ref			
Nevirapine based	1.79 3.52	0.9 –	7.93 – 27.86	2.26		
Second line drug	0.86 4.86	0.15 –	1.02 – 11.8	0.09		
Pill count rate			0.012*			0.264
Good adherence	ref		ref			
Fair adherence	0.3	0.1 – 0.93	0.43 – 1.69	0.11 –		
Poor adherence	1.93 4.03	0.92–	1.65 – 5.01	0.54		

***: p < 0.05.**

Discussion

In this cross-sectional study, a relatively large proportion of the 250 CLHV (38%) had virological non-suppression after being on ART for a mean period of 64 ± 3.0 months. Female gender, having a previous history for TB treatment, severe CD4⁺ immunodeficiency status at study recruitment and a NVP-based regimen were associated with virological non-suppression. Some factors identified in other studies such as adherence to ART, clinical stages 3 and 4, parent's educational level and their employment status were not significant in this current study.

As antiretroviral access continues to expand in resource-limited countries like Ghana, monitoring response to ART by the use of VL measurements is critical in determining the effectiveness of ART in the population.^{29,173} The Sub-Saharan African region's prevalence for virological non-suppression (>1000 copies/ml) in children who have been on ART for at least 6 months ranges from 13% to 44%.^{8,30,31} A virological non-suppression rate of 38% found in this study increases the risk for the emergence of ART resistance and subsequently failure of the ART regimen, necessitating a switch to second, or later third line treatment.⁸ This ultimately would result in an increase in morbidity and mortality of the CLHV and cause the spread of resistant viruses.⁸ Given these consequences, VL monitoring per national guidelines should be routinely done in all children on ART and those identified as being virologically non-suppressed, should have adherence counselling and then a repeat viral load level to confirm if they have virological failure. Once virological failure has been confirmed then the various drug switch should occur according to Standard Treatment Guidelines outlined by NACP.⁶

The rate of non-suppression observed in this study could be due to a number of reasons. Firstly, VL monitoring has been a programmatic challenge at the Paediatric HIV clinic in the study setting, characterized by frequent interruptions in the availability of resources required by the laboratory, resulting in erratic provision of services. Without close monitoring of VL levels, the patients are at risk of unrecognized virological failure as continuing a failing regimen is associated with accumulation of HIVDR variants.¹⁶⁸ Adequate funding and improved logistics management to ensure uninterrupted VL testing in the laboratory would boost the implementation of the VL monitoring protocol that exists in the clinic.

We observed a relatively high proportion of patients with virological non-suppression (38%). This translates to a virological suppression rate of 62% and is similar to the estimate made by Ghana in respect of its achievement of the third 90 of the UNAIDS 90-90-90 targets. This shows that more effort should be made as a country in achieving the current 95-95-95 targets which has been proposed by UNAIDS with the purpose of ending AIDS by 2030.³²

The prevalence of children with detectable viral loads above 20 copies/ml but less than 1000 copies/ml (low level viraemia (LLV)) in this study was 23%. This group of patients are denoted as 'non-failures' and WHO does not make any provision for the management of LLV. These group of individuals will not receive any follow-up VL for at least six to 12 months and thus risk continuing on a failing regimen for considerable time. There is therefore the need to design algorithms for patients with LLV to have more frequent VL monitoring as literature has shown the emergence of high-level resistance in this group of individuals.³³

We observed that females were 2.5 times more likely to have virological non-suppression as compared to males. This phenomenon was similar to the study by Muri *et al*,³⁴ in Tanzanian children, whereby females were also 2.5 more times likely to have virological non-suppression. On the contrary, some studies have reported that males had increased odds of virological non-suppression,^{13,35} whilst other studies however found no association between sex and virological non-suppression.³⁶ The role of gender in virological suppression could be biologic according to authors such as Njom *et al*.³⁷ The relationship of virological suppression and gender is therefore inconclusive and requires further studies.

A third of the study population had been previously treated for TB. Furthermore, having a history of previous TB treatment increased the odds of having virological non-suppression by as much as five times. These findings are in agreement with studies reported by Ahoua *et al*,³⁸ and by Rajin *et al*.³⁹ On the other hand, it has been recently reported that children who had a history of TB co-infection had better virological outcomes.¹³ Reasons for this could be due to the close monitoring, frequent clinic visits and adherence support, adopted as part of TB treatment offered at the sample sites. The association of a previous history of TB and virological non-suppression in this current study could be due to the increased pill burden and drug-drug interactions between the medications that these patients are on. The significance of TB comorbidity on the occurrence of virological non-suppression buttresses the need for the prioritization of VL monitoring and adherence support in co-infected patients as well as patients who have a history of previous TB.

The odds of virological non-suppression was almost eight times more likely in study participants whose current drug regimen was NVP-based as compared to a study participant who had an EFV-based regimen. The findings of this study is consistent with current literature that shows that patients on NVP-based regimens experience more virological failure than patients on EFV-based regimens.^{18,19} The use of regimens containing NVP is associated with a low genetic barrier of drug resistance and a higher risk of baseline resistance in cases where NVP was used as prophylaxis in the babies for Prevention of Mother To Child Transmission (PMTCT). This current study however did not evaluate prior NVP exposure. Our findings support the current ART guidelines being used at the HIV clinic at KBTH which is to phase out NVP based regimens and replace with LPV/r or EFV regimens for children less than 20 kg. Current guidelines recommend a Dolutegravir (DTG) based regimen as the preferred first-line for children weighing at least 20kg. Hopefully with the introduction of DTG and its scale up, the non suppression due to certain antiretroviral drugs such as NVP will be reduced.

We observed that study participants found to have severe CD4⁺ immune suppression status at the time of study recruitment were 25 times more likely to have virological non-suppression. These findings are in congruence with studies reported by Jobanputra *et al*,³⁶ among children in Swaziland and by Izudi *et al*,⁴⁰ among children in Northwestern Uganda where it was found that patients with low CD4⁺ count values at study recruitment were more likely to have virological non-suppression. This finding is expected and supports the knowledge that viral suppression leads to immune recovery and could reflect the fact that those study participants who were virologically suppressed had a chance to reconstitute their immune systems for their CD4⁺ counts to increase.⁴¹ This finding also supports early initiation of ART in children and according to the current ART guideline in Ghana, all children confirmed to have HIV diagnosis after birth are started on ART regardless of the CD4⁺ count.

There was no association between parent-educational level, employment status of parent and virological non-suppression in this study. This is in agreement with a Danish HIV Cohort reported by Legarth *et al*⁴² which also showed no association between education level and virological non-suppression. This finding is however in

contrast to a study reported by Mensah *et al*⁴³ in Ghana, in which a child with an unemployed caregiver was five times more likely to have virological non-suppression. There is substantial evidence on the socioeconomic inequalities in the treatment outcomes of chronic diseases like HIV. This current study could not confirm association between employment status and virological non-suppression. This observation could be due to the fact that for almost a third of study participants, the educational and employment status of parents was not known.

Studies on the relationship between self-reported adherence to ART and virological non-suppression have shown inconsistent results.^{20,44} In this study, adherence level measured by pill count was not associated with virological non-suppression. On the other hand in a clinical trial reported by Intasan *et al*,⁴⁵ in Cambodian children, non-adherence was associated with virological non-suppression. The measure of adherence used in the study by Intasan *et al*,⁴⁵ was however the 3 day self-report by caregiver. In a more recent research by Natukunda *et al*,³¹ in adolescents, reported in 2019, more than 70% of adolescents who experienced virological non-suppression were sufficiently adherent as measured by pill count (adherence >95%). On the other hand, there are also studies whereby poorly adherent patients maintained undetectable VL.^{44,46}

The strength of this current study is that it did not only determine the prevalence of virological non-suppression but explored factors associated with the phenomenon in children. In the absence of drug resistance testing information, close monitoring of VL levels, multidisciplinary support and prompt clinical judgment are key in ensuring children who have failed treatment are appropriately transitioned to second line therapy. Ultimately, 'an ounce of prevention is better than a pound of cure.'

Limitation: The reliance on self-reported data as a measure of adherence, which may be affected by recall and social desirability bias. Analysis of baseline VL and CD4⁺ count was not available for some of the subjects and hence analysis on baseline VL and CD4⁺ could not be done for those patients. This is because VL monitoring was started in April 2011 (as a national policy) and hence all children above eight years of age did not have the opportunity of having a baseline VL level done.

Conclusion

The high rate of virological non-suppression is consistent with findings in other countries in Sub-Saharan setting and emphasizes the great challenge to successfully suppressing HIV in paediatric patients and reinforces the need for regular monitoring of viral load levels in children. Patients on ART with active TB and those with a history of previous TB should be prioritized for more regular VL monitoring (6 monthly) as the national guidelines advocate for yearly monitoring of viral load for patients whose viral load levels are suppressed. Further research should focus on determining resistance patterns in this study population.

Declarations

Ethics approval and consent to participate

Ethical approval (KBTH-IRB/ 00060/2017) was obtained from the Institutional Review Board of Korle Bu Teaching Hospital, Accra, Ghana. An informed consent was obtained from parents or legal guardians for each minor participant prior to enrolment to participate in the study. All procedures performed involving study participants

were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Consent for publication

Not applicable.

Availability of data and materials

The data sets used and analysed during this study are available with the corresponding author on request.

Competing interest

All authors declare that there are no competing interests.

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Authors' contributions

AKAA contributed to conception and study design, acquisition of data, analysis and interpretation of data and drafting of the manuscript. AK, BG, LR contributed to study design, interpretation of data and substantively revised it. SO contributed to acquisition of data. SA contributed to laboratory testing. YA contributed to analysis of data and interpretation of data. AEY contributed to analysis of data, interpretation of data and substantively revised it. KWCS contributed to conception and study design, interpretation of data and substantively revised it. All authors read and approved the final manuscript.

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Abbreviations

ABC -	Abacavir
AIDS -	Acquired Immunodeficiency Syndrome
AOR -	Adjusted Odds Ratio
ART -	Antiretroviral Therapy
CD4 -	Cluster of differentiation 4

CD4% - CD4 percentage

CLHV Children Living with HIV

DTG - Dolutegravir

EFV Efavirenz

ELISA - Enzyme-linked immunosorbent assay

FDA Food and Drug Administration

HIV - Human Immunodeficiency Virus

HIV VL HIV viral load

KBTH - Korle Bu Teaching Hospital

LMIC - Low- and middle-income countries

LLV - Low level viraemia

LPV/r - ritonavir boosted lopinavir

NACP - National AIDS Control Programme

NVP - Nevirapine

PCR - Polymerase Chain Reaction

PI - Protease Inhibitor

SPSS - Statistical Package for Social Sciences

TEN - Tenofovir

TB - Tuberculosis

VL - HIV-1 RNA Viral Load

U.O.R - Unadjusted Odds Ratio

27 WHO - World Health Organization

ZDV - Zidovudine

3TC - Lamivudine

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Table 1

Table 1: Baseline characteristics of patients according to virological suppression status

	VL at study recruitment (copies/ml)		Total	χ^2	P value
	Suppressed (≤ 1000)	Non suppressed (> 1000)			
Characteristics	n (%)	N (%)			
Age category				1.10	0.576
<5 years	16 (53.3)	14 (46.7)	30 (100.0)		
5 to <10 years	44 (61.1)	28 (38.9)	72 (100.0)		
10 to 15 years	94 (63.5)	54 (36.5)	148 (100.0)		
Sex of child				4.43	0.035*
Female	64 (54.7)	53 (45.3)	117 (100.0)		
Male	90 (67.7)	43 (32.3)	133 (100.0)		
Primary caregiver relationship to subject					
Mother	45 (39.1)	70 (60.9)	115 (100.0)	2.15	0.499
Father	12 (48.0)	13 (52.0)	25 (100.0)		
Guardian	50 (45.5)	60 (54.5)	110 (100.0)		
Educational status of father				4.16	0.527
None	11 (57.9)	8 (42.1)	19 (100.0)		
Basic (Primary/JHS/Middle)	36 (40.0)	29 (60.0)	65 (100.0)		
Secondary	53 (64.6)	29 (35.4)	82 (100.0)		
Tertiary	19 (73.1)	7 (26.9)	26 (100.0)		
Educational status of mother				1.27	0.938
None	15 (55.6)	12 (44.4)	27 (100.0)		

Basic (Primary/J.HS/Middle)	59 (64.0)	35 (36.0)	94 (100.0)		
Secondary	23 (63.9)	13 (36.1)	36 (100.0)		
Tertiary	8 (72.7)	3 (27.3)	11 (100.0)		
Occupational class of father				φ	0.541
Professional	2 (62.5)	0 (37.5)	2 (100.0)		
Other	115 (61.5)	72 (38.5)	187 (100.0)		
Unemployed	2 (76.5)	1 (23.5)	3 (100.0)		
Occupational class of mother				φ	0.73
Professional	0 (0.0)	0 (0.0)	0 (100.0)		
Other	90 (59.5)	61 (40.5)	151 (100.0)		
Unemployed	11 (66.7)	6 (33.3)	17 (100.0)		

CLINICAL AND LAB VARIABLES

TB treatment in the past				2.74	0.098
no	116 (64.8)	63 (35.2)	179 (100.0)		
yes	38 (53.5)	33 (46.5)	71 (100.0)		
WHO stage at ART initiation				1.82	0.611
Stage 1	64 (66.0)	33 (34.)	97 (100.0)		
Stage 2	42 (61.8)	26 (38.3)	68 (100.0)		
Stage 3	35 (55.6)	28 (44.4)	63 (100.0)		
Stage 4	13 (59.1)	9 (40.9)	22 (100.0)		
Baseline VL (copies/ml)				Φ	0.751
<10000	22 (73.3)	8 (26.7)	30 (100.0)		
10,000 to 99,999	13 (60.0)	9 (40.0)	22 (100.0)		
100,000 to 499,999	8 (66.7)	4 (33.3)	12 (100.0)		

> 499,999	7 (70.0)	3 (30.0)	10 (100.0)		
Baseline					
CD4+ Immune suppression status (overall)				1.36	0.71
Severe	23 (65.7)	12 (34.3)	35 (100.0)		
Advanced	17 (68.0)	8 (32.0)	25 (100.0)		
Mild	12 (66.7)	6 (33.3)	18 (100.0)		
none	90 (61.2)	57 (38.8)	147 (100.0)		
CD4+ Immune suppression status at study recruitment (overall)				Φ	<0.001*
Severe	7 (29.2)	16 (66.7)	24 (100.0)		
Advanced	1 (38.9)	11 (61.1)	18 (100.0)		
Mild	12 (52.1)	11 (47.8)	23 (100.0)		
normal	115 (73.3)	44 (26.7)	165 (100.0)		
ART RELATED VARIABLES					
Duration of ART				2.15	0.828
<12 months	17 (53.1)	15 (46.9)	32 (100.0)		
12-23 months	19 (61.2)	12 (38.8)	31 (100.0)		
24-36 months	15 (65.2)	8 (34.8)	23 (100.0)		
36-47 months	13 (65.0)	7 (35.0)	20 (100.0)		
49-50 months	10 (52.6)	9 (47.4)	19 (100.0)		
>59 months	80 (64.0)	45 (36.0)	125 (100.0)		
Current ART regimen				5.32	0.07
Nevirapine based	34 (50)	34 (50.0)	68 (100.0)		
Efavirenz based	114 (65.9)	59 (34.1)	173 (100.0)		
Second line drug	6 (66.7)	3 (33.3)	9 (100.0)		

Adherence (Pill count percentage rate)				7.99	0.018*
	29		58		
Poor adherence (85%)	(50)	29 (50.0)	(100.0)		
	32		41		
Fair adherence (85%-94%)	(78.0)	9 (22.0)	(100.0)		
	93		151		
Good adherence (≥ 95%)	(61.6)	58 (38.4)	(100.0)		
Person responsible for child's medication				4.55	0.336
	82		132		
Mother only	(62.1)	50 (37.9)	(100.0)		
	13		25		
Father only	(52.0)	12 (48.0)	(100.0)		
	5		12		
Both parents	(41.7)	7 (58.3)	(100.0)		
	9		34		
Grandparents	(26.5)	25(73.5)	(100.0)		
	11		47		
Others	(23.4)	36 (76.6)	(100.0)		

χ^2 : Pearson's chi-square

#: row percentage

*: $p < 0.05$.

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