International Journal of Scientific Research and Engineering Development-– Volume 6 Issue 1, Jan-Feb 2023

Available at www.ijsred.com

RESEARCH ARTICLE OPEN ACCESS

Factors Contributing to Viral Load Non-Suppression Among Adolescents on Antiretroviral Therapy Services in Mbarara City

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Abstract

Introduction. Viral suppression among patients enrolled on ART is important for timely detection of treatment fai1ures, and identification of patients who need advanced adherence counseling. Thus, viral load is a critical indicator for HIV treatment to the viral load testing request form version for Uganda, with interest in establishing success or suspected failure for the ART treatment outcome. This study was designed to investigate the prevalence and factors associated with viral load non-suppression among HIV infected adolescents on ART seeking health services from health facilities within Mbarara city.

Methods: This studywas a retrospective study that employed both quantitative and qualitative methods of data collection and was carried out among 318 HIV-positive adolescents seeking adolescent HIV health services from health facilities within Mbarara city.Probability Proportional to Size (PPS) sampling procedure was used to allocate the sample to the different health facilities offering HIV care.

A structured questionnaire for face-to-face interviews complemented by routine clinical data retrieved from medical ART records was used. Also, key informant interviews were conducted with health staff at the health facilities using interview guides. Bivariate analysis was conducted to determine association between viral load non-suppression and socio-demographics or clinical factors among the adolescents. Logistic regression was used to determine the association by which socio-demographic and clinical factors influence viral load non-suppression. Odds Ratios (ORs) were used for statistical associations at 95% confidence interval considering statistical significance for p-values less than 0.05.

Results: HIV viral non-suppression among (n=318) adolescents was at 28%. The study findings revealed that adolescents who reported not disclosing their HIV status had a positive association with viral load non-suppression (□²=30.836, P-Value=0.000). Similarly, having ever had active TB in last 12 months had a significant association with viral load non-suppression (□²=300.000, P-Value=0.000). Furthermore, adolescents who had a poor level of adherence were positively associated with viral load non-suppression (□²=300.000, P-Value=0.000). Adolescents who were on the first line were 10.90 times less likely to have virological non-suppression when compared with adolescents on the second line of treatment (AOR 10.90 [95% CI 3.79–31.41], p<0.001). Additionally, adolescents who had their parents alive were 1.47 times less likely to have virological non-suppression when compared to adolescents who never had their parents alive (AOR 1.47 [95% CI 1.01–3.02], p < 0.05).

Conclusion: In conclusion, this study found that adolescents continue to face worse HIV viral load outcomes. The determinants of viral load non-suppression among adolescents are unique and thus require unique interventions.

Key Words: Adolescents, virologic non-suppression, antiretroviral treatment, HIV/AIDS, Uganda.

Background

Adolescence is a complex development phase of marked psychosocial, behavioral, physiological and cognitive changes (Jaspan et al., 2009; Li et al., 2010) that exacerbate the challenges of an HIV-positive status and the requirement to adhere to a structured treatment regimen. It is a time when there is hyperawareness of physical appearanceand also a time of experimentation, risk-taking and significant peer influence with a need to assert an individual identity that is distinct from caregivers (Holmbeck, 1999).

The phase is often associated with deviations from expected or prescribed behavior. These factors may complicate adolescents' transition toward taking responsibility for managing their illness, ART adherence and clinic appointment attendance. Adolescents have been found to have poor adherence to antiretroviral therapy, with one study showing a decrease in adherence as children moved into adolescence (Foster &Filder, 2010). In addition, low levels of virological suppression, increased risk of virological failure, lost to follow-up (LTFU) and death have all been described (Bakanda et al., 2011).

Despite many decades of continuous fight, Human immunodeficiency virus (HIV) is still one of the major global health issues, having claimed more than 35 million lives so far, with the African Region in particular being the most affected with 25.7 million people living with HIV in 2017 (UNICEF, 2019; WHO, 2019). As the momentum in the efforts to control the pandemic rises, the global commitment to ending HIV/AIDS epidemic was set by the United Nations (UN) Assembly for 2030 (UNICEF, 2019).

Reducing the incidence and providing antiretroviral treatment to the infected people are key in the progress and achievement of this goal. A great stride in the journey towards ending HIV/AIDS is the ambitious treatment targets set by the Joint United Nations Programme on HIV/AIDS (UNAIDS), the 90–90–90 strategy by 2020. This goal stipulates that by 2020, 90% of all people living with HIV will know their HIV status; 90% of all people with diagnosed HIV infection will receive sustained antiretroviral therapy; and 90% of all people receiving antiretroviral therapy will have viral suppression (UNAIDS, 2016). Achieving these targets is especially challenging for developing countries where limited access to health care, drug availability and adequate provision of viral load monitoring tools and other programmatic issues need to be addressed.

According to the World Health Organization (WHO) an adolescent is an individual between the ages of 10-19 years inclusive (WHO, 2012). In 2018, about 1.6 million [1.1 million-2.3 million] adolescents between the ages of 10 and 19 were living with HIV worldwide. Adolescents account for about 4% of all people living with HIV and about 11% of new adult HIV infections. Sub-Saharan Africa is one of the regions with the highest numbers of HIV-positive adolescents where about 1.5 million [970,000-2.0 million] (89%) of the 1.6 million adolescents living with HIV, live (UNICEF, 2019).

Of the 89% HIV-positive adolescents in sub-Saharan countries, 60% of them are girls. Adolescent girls are two to three times more likely to be infected with HIV than boys of the same age group. However, HIV does not only affect sub-Saharan Africa, and in 2018, 18% of adolescents newly infected with HIV lived outside of the region (UNAIDS, 2016). In Uganda, of the 130,000 adolescents 10 to 19 are living with HIV,only 21,641 (17%) of adolescents living with HIV were active in HIV chronic care,12,695 of the 43,333 (29%) ART eligible adolescents were on ART and about 17 % of HIV care clinics offer adolescent friendly services(MOH, 2019).

Viral suppression among patients enrolled on ARTis important for timely detection oftreatment fai1ures, and identification of patients who need advanced adherence counseling(WHO, 2016).Effective ART leads to viral suppression, which in turn, restores immune function, reducesHIV-related morbidity, prolongs survival, and improves quality of life of HIV patients and alsoprevents transmission of HIV to their uninfected sexual partners (Evanset al.,2013; WHO,2016). Viral load non suppression occurs when antiretroviral therapy (ART) fails to suppress and sustaina person's viral load to less than 1000 copies/ml (MOH, 2016).

High levels of adherence to ART are needed to ensure viral suppression and prevention of theemergence of HIV drug resistant virus (Paterson et al., 2000). It is widely reported thatadolescents find consistent, long-term adherence to any medication difficult, and ART is noexception (Hanghj&Boisen, 2014). Compared to adults, adolescents on ART are more likelyto have an unsuppressed viral load and more likely to fail virologically, as reported by two South African studies (Evans et al.,2013; Nglazi et al.,2012). Another study in Uganda foundthat children (0-18 years) are almost twice as likely to have viral load non suppression compared toadults (Kamya et al.,2007).

According to the 2016 edition of guidelines on the use of antiretroviral drugs for treating and preventing HIVinfection in Uganda, a viral load test should be carried out at 6 and 12 monthsafter initiation of ART and annually thereafter if the viral load is less than 1,000 copies/ml(MOH, 2016). In the same guidelines; treatment failure is defined as a persistently high viralload greater than 1,000 copies/ml (two viral loads measured within a 3-month interval withadherence support between measurements), after at least 6 months of using ART (MOH, 2016).As per WHO clinical treatment guidelines, those with treatment failure should be switched toappropriate second-line or third-line ART regimen, after enhanced adherence counseling(WHO, 2013).

Viral load non-suppression (VLNS) is the worldwide cause of antiretroviral therapy (ART) failure and yet over 3 million adolescents in low- and middle-income countries receive ART (UNAIDS, 2016). According to the guidelines of the World Health Organization (WHO) for the treatment of human immunodeficiency virus (HIV) infection recommend that viral loads of individuals receiving ART be measured every 6 months to detect viral replication and confirm treatment failure whenever it occurs(World Health Organization, 2010). WHO's guidelines for the treatment of HIV infection

recommend that a viral load of > 5000 copies of viral ribonucleic acid (RNA) per ml be taken as indicative of viral load failure (Boatman et al., 2019).

The Ugandan guidelines recommend that viral load testing should be done 6 months after initiating ART and thereafter annually for people who have achieved viral suppression (UNICEF, 2019). However, people with detectable viral loads undergo targeted intensified adherence support for 6 months followed by confirmatory viral load testing in order to differentiate poor adherence from treatment failure. Those with treatment failure as defined by two detectable viral load measurements above the threshold are switched to second-line ART(UNICEF, 2019).Uganda ranked among the top 20 high burden countriescontributing 5% of AIDS-related deaths among adolescentsin 2014 (Bulega et al., 2017). The deaths are attributed to thelate diagnosis and poor access to treatment with most perinatally infected children starting treatment later inlife.

In 2014, the Joint United Nations Programme on HIV/ AIDS (UNAIDS) set new targets towards elimination of HIV, including diagnosis of 90% of HIV infected individuals, access to treatment for 90% of identified HIV infected persons, and 90% viral suppression among those initiated on treatment (MOH, 2019). These targets have since been adopted by several countries including Uganda. Thus, viral load is a critical indicator for HIV treatment to the viral load testing request form version for Uganda, with interest in establishing success or suspected failure for the ART treatment outcome. Despite the increasing number of HIV+ patients accessing ART, there is limited information about non-suppression rates amongst the different groups of people enrolled in care in Uganda and many resources limited settings.

Methods

Study Design

This was aretrospective study that employed both quantitative and qualitative methods of data collection and was carried out among HIV-positive adolescents seeking health servicesfrom all the health facilities within Mbarara city offering HIV adolescent care. The cross sectional design was preferred because it enabled the researcher to target a large group of respondents to obtain information without making a follow up of the respondents once information from them is obtained (Sekaran & Bougie, 2013). The researcher sought convergence across qualitative and quantitative methods to minimize biases and weaknesses that reside in the use of one method

Study Setting

The study was conducted from all health facilities offering HIV adolescent care within Mbarara city. Mbarara cityis 266 km southwest of Kampala the capital city of Uganda. The catchment population is estimated at over 400,000 people (UBOS, 2018). The majority of the HIV positive patients come from Mbarara city. The ART clinics operate on an outpatient basis offering services such as health education, routine counseling and testing for HIV at risk adolescents.

Study Population

The target population for the study consistedofHIV-positive adolescents seeking health services from health facilities within Mbarara city. The ART clinic health care workers who are directly involved in adolescent care will be considered as key informants in the study. These are the people the researcher believed had information concerning the viral load non-suppression. The study populationincluded all adolescents aged 10-19 yearson ART treatment and Care Program in Mbarara city.

Inclusion and exclusion criteria

This study included adolescents aged between 10-19 years seeking ART from the study area and had stayed for at least six months in ART care; those who were on ART and consented/assented to participate in the study; and those who had valid viral load test result at the most recent viral load test during measurement year. Those with less than 6 months follow up from the date of ART initiation and did not have at least one viral load test result after 6 months of ART were excluded from the study.

Sample Size and sampling procedure

The sample size was estimated using a standard formula by (Kish & Leslie, 1965), with 5% marginal error and 95% confidence interval to arrive at a sample size of303 participants. The sample size was then adjusted for missing data, and non-response; Adjusted sample size was computed as 318 respondents. Probability proportionate to size sampling was used in this study because of the varying ART clinic sizes. This was aimed at ensuring that adolescents from larger ART clinics had the same probability of being included in the sample as those in smaller.

Probability Proportional to Size (PPS) sampling procedure was used to allocate the sample to the different health facilities offering HIV care. A list of all the facilities offering adolescent HIV care within Mbarara city together with their number of adolescents on ART was drawn per health facility. The overall total number of adolescents on ART was then be divided by the number of adolescents

in HIV care per facility to get the sampling interval. A random number (r) was then be randomly selected from the charts. The adolescents whose charts are selected were then be contacted for consent/assent before reviewing them. After obtaining consent/assent, theselectedcharts from the facility were then be reviewed until the number allocated per health facility is attained.

Charts with a lot of missing data were excluded and instead the subsequent chart picked for review. At each of these facilities, a key informant interview was conducted with the ART Clinic Manager (In charge) directly involved in provision of adolescent ART treatment care to identify the clinical factors related to viral load non suppression among adolescents.For the health facilities, a census of the total number of health units offering adolescent friendly ART treatment was done. All thesystematically sampled patient charts and ART Clinic registers from thepurposively selected health facilities were reviewed to determine viral load non suppression.

The number of adolescents to be interviewed at each health facility was determined using the proportionate sampling, see table 1.

Purposive sampling was used to select participants for the in-depth interviews to share views and experience. These included ART clinicians especially those handling adolescents, counselors and peer educators. Priority was given to HIV positive adolescent peers where they support adolescent clinics. This is because they interact with fellow HIV positive adolescents and therefore understand them in-depth. This makes information collected more valid, reliable and representative.Viral non suppression was measured in terms of viral RNA copies/ml of blood, age, sex, duration of treatment, treatment line (first, second, third), CD4 < 500 and having active TB.

Data collection

The investigator engagedtwo research assistantsto extract data from the electronicmedical records (EMR). The two research assistants were trained on how to collect and fill out the data tools, obtaining informed consent and assent, and observation of all the ethical considerations. A structured questionnaire for face-to-face interviews complemented by routine clinical data retrieved from medical ART records was used.Accordingly, all charts containingdetailed information about patients who are on ARTfrom were reviewed. The investigator closely monitored the whole datacollection process on a daily basis. Adherence to treatmentwas determined using the World Health Organization (WHO)definition in the follow-up chart. Thus, poor adherence totreatments is defined as patients taking ≤95% of the recommendedregimens.

During qualitative data collection, key informant interviews were conducted with health staff at the health facilities using interview guides. This method was applied toonly select health facility ART clinic in charges and this gave the researcher anopportunity to explore information about the research questions to compliment andcorroborate data from quantitative design.

Therefore,in depth interviews were conducted with 10 key informants, of which these were health workers that were purposively sampled from Medical Officers or Clinicians administering ART or any other experienced health worker providing adolescent HIV services like ART counselors and pharmacists.

Data analysis

Quantitative Analysis

The quantitative data was cleaned, edited, coded and entered into the computer using Epi Data and then exported to STATA v15 for analysis.Continuous variables such as age were categorized accordingly and proportions and percentages were used for categorical variables. Analysis was conducted at three levels; univariate, bivariate and multivariate levels. Bivariate analysis was conducted to determine association between viral load suppression and independent variables. Odds Ratios (ORs) were used for statistical associations at 95% confidence interval considering statistical significance for p-values less than 0.05.

Qualitative Analysis

The audio recordings from key informants were listened to carefully and transcribed, and to verify the quality of transcription, the tapes were double transcribed. The data was analyzed by grouping related responses into themes and subthemes in accordance with the study objectives. Key statements were quoted verbatim to give the exact meaning using the narrative qualitative analysis approach(Anderson, 2010).

Results

Proportion of adolescents with non-suppressed viral load

Figure 1 shows that 83 (28%) of the adolescents had unsuppressed viral load whereas 217 (72%) had a suppressed viral load.

Association between virological non-suppression of adolescents on ART stratified by socio-demographic and clinical characteristics.

Table 2 presents results of association between virological non-suppression of adolescents on ART stratified by socio-demographic and clinical characteristics. The study findings reveal that adolescents not having their parent(s) alive had a significant relationship with viral load non-suppression (□²=14.883, P-Value=0.000). also, adolescents who reported not disclosing their HIV status had a positive association with viral load non-suppression (□²=30.836, P-Value=0.000). similarly, having ever had active TB in last 12 months had a significant association with viral load non-suppression (□²=300.000, P-Value=0.000). furthermore, adolescents who had a poor level of adherence were positively associated with viral load non-suppression (□²=300.000, P-Value=0.000).

Clinical factors associated with viral load non-suppression among HIV infected adolescents.

In multivariate analysis, adolescents who on the first line were 10.90 times less likely to have virological non-suppressionwhen compared with adolescents on the second line of treatment (AOR 10.90 [95% CI 3.79–31.41], p<0.001). Additionally, adolescents who had their parents alive were 1.47 times less likely to havevirological non-suppression when compared to adolescents who never had their parents alive (AOR 1.47 [95% CI 1.01–3.02], p <0.05). See table 3

Qualitative results

The different health providers who participated in these interviewsincluded HIV Clinical Care Coordinator, Clinicians, Nursing Officers, Counsellors andPharmacist.

On the socio-demographic factors, one of the key informers emphasized that;

"Majority of adolescents (almost over 80%) have single parents, others staying withguardians even when both parents are alive. This affects suppression because some of themdon't have treatment supporters to remind them. For example, school going children are morelikely to forget their medicines when rushing for school or classes since they have no one toremind them.If one is staying with members who take same drugs, it's more likely that both take theirmedications at the same time. However, change of family members (moving from one caretakerto another) may affect their suppression if the caretaker has never been counselled or educatedon the effect of adherence."

KI, Clinical Care Coordinator]

This is in line with the findings of the study where majority adolescents did not have bothparents. The presence of one or both parents, same family member taking ARVs as theadolescent and attending school is thought to have influence on viral load suppression of anadolescent.The level of education of the caretaker or adolescent is believed to have an effect on adherenceand viral load non-suppression especially for adolescents.

"*Most caretakers who are highly educated feel they know a lot and don't want to spend a lot of time being told what to do, and they end up doing things contrary to the requirements. Those whoare illiterate tend to be rigid and need a lot of effort to accept changes especially on number ofpills. However, with constant counselling, they are able to adjust. Middle class caretakers tend toreadily accept all advice in case there is need for change*"

[KI, Nursing Officer]

This finding was also emphasized by one of the key informers who said;

"*As the adolescents grow older, due to fear of stigma, they fail to take their medicines in time or stop taking them. However, they continue to pick the medicines from the health facility and keep them. At times wherethere is erroneous dispensing of wrong medicines, the educated patients easily notice and askwhy they got different drugs. Illiterates come back when they have reacted to the medicines*."

[KI, Counsellor].

Religion is another socio demographic factor that has been associated with viral load non-suppression. On matters of religion, another informant had this to say;

"*Born again individuals tend to abandon medicines after being prayed for. Sometimesthey bring back their drugs claiming they were prayed for and they are now declaredhealed or free of HIV. However, there are Born-again adolescents whose pastors advise that they should continue withtheir medication even after prayers*"

[KI, Clinician]

Age at initiation on the ART regimen is also said to have effect on the viral load non-suppression ofadolescents.

"*Adolescents who start medicines early adhere well in the start years. As they progress, they gettired of the medicines and easily default. But disclosure is one of the major concerns. Ifadolescents are not disclosed to early, first they start asking why they are taking medicines, tryto experiment by not taking and are likely to default. Adolescents who start at a very early age,their adherence is better*

and they adhere completely if they have been disclosed to."

[KI, Clinician]

On the typeof regimen and viral load non-suppression, one informant had this to say;

"*Some adolescents are scared by the size of the pill; the larger the size, the less some individuals adhere."*

[KI, Pharmacist]

On client factors, privacy during counselling has been emphasized as one of the forgotten butimportant factor that would influence adherence and suppression status.

"*I would rate our environment here as average. There is lack of space for counselling adolescentshence no privacy on adolescent information shared. However, the adolescents' file informationis kept confidential and inaccessible without permission*."

[KI, Clinician]

When asked if the appointment system is convenient to serve adolescent needs; one keyinformant said;

"*There is room for discussion if adolescents give realistic reasons. We discuss with adolescentsattending boarding schools and fix an agreed appointment date. For those at schools and arestable, up to 3 months of medicine refills are given. We still experience challenges with pooradherence and requests for longer refills still exist*."

[KI, Counsellor]

Viral load suppression is said to be better if staff have acquired training in delivery of adolescentservices. On this subject, key informants narrated;

"*Only one clinician has been trained in adolescent services at the hospital where majorityadolescents are enrolled on ART. Those who were trained recently in adolescent services at themain hospital are not serving on the HIV clinic. There is still a gap to conduct targeted trainingin adolescent friendly services. Even for pharmacists, there were no special trainings on how tohandle different age groups when dispensing drugs*."

[KI, Clinician]

Like children, adolescents require parental consent for medical treatment until they reach the legal age of consent (18 years). Adolescents can be given information and education but cannot receive

care without parental consent. Yet, some adolescents below 18 years of age are capable of making their own care decisions and need to be involved in their own care.

"For example, we were told that anybody below the age of 18 [years] is a minor. There are issues of consenting towards some of these services, including testing, or providing other services, where an adolescent need to come with a parent or a guardian, so that the issue of consent is adhered to. That is a challenge in terms of policy."

[KI, Clinical care coordinator]

Discussion

Proportion of adolescents on ART with virologic non-suppression

This study found that 28% of the adolescents on ART had viral non-suppression during the study period. The virologic non-suppression rate of 28% found in this study is almost comparable to the national age-specific rate of 27.5% among adolescents in 2017/2018 (UAC, 2018). A cross-sectional study by Natukunda et al., (2019) in Uganda found the virologic non-suppression prevalence among adolescents to be 34.5%, which is a little higher than this study's rate. This study's rate is also higher than that reported in South Africa (19%) (Boerma, 2016). The overall proportion of virologic non-suppression was higher compared to the study conducted in Uganda 11% (Bulage et al., 2017), Systematic review on viral non-suppression rate in low or middle-income countries of the pooled estimate had 16% (McMahon et al., 2013). Equally, a study conducted among HIV-positive children in rural Zambia found that only 11.5% of the children were virologically non-suppressed after six months of treatment (Van Dijk et al., 2011).

Similarly, another study conducted in Zimbabwe found that 19% of the children were virologically non-suppressed, although the study was done in a hospital that specialized in managing opportunistic infections and managing complicated referrals of HIV patients on second- and third-line treatment, which could explain the lower proportion of non-suppression among the children (Moyo et al.,

2020). Also, findings from a study conducted among adolescents living with HIV in Cambodia found that 23.2% had virologic non-suppression (Chhim et al., 2018). More so, findings from a study done in central Uganda among HIV positive adolescents on ART medications revealed that 23% had virologic non-suppression (Nabukeera et al., 2021).

The findings of this study are lower than those of a study conducted in Ghana which revealed that 38% of the adolescents had a virologic non-suppression (Afrane et al., 2021). Another study among adolescents less than 19-years-old in Rwanda found a viral non-suppression rate of 39% (Mutwaet al., 2014). Another study conducted in Zimbabwe showed that 35.1% adolescents living with HIV had virologic non-suppression (Simms et al., 2021). Adolescents in Uganda, therefore, show a higher rate of viral non-suppression and are lagging behind other age groups in achieving the 95–95–95 targets, making them a weak link in the collective effort to reach the goal above (UAC, 2018).

The possibility of having good adherence yet with poor viral outcomes cannot be ruled out in a setting like Uganda where treatment options are not regularly updated and there is limited routine ART resistance testing (WHO, 2017). Besides only reporting the proportion of adolescents with non-suppressed viral loads, the present study also identified independent predictors of viral non-suppression among this critical population. The findings in the study suggest the need for HIV clinical services to design and implement targetedinterventions with a particular focus on male gender, comorbidities, adolescents on second line ART and those on longer duration of ART.

Socio-demographic factors associated with viral load non-suppression among HIV infected adolescents

In this study, adolescents who knew their own HIV status but had not told anyone else were more than one times more likely to have virological non-suppression. Similarly, in South Africa, non-disclosure was associated with virologic non-suppression (Cluver et al., 2015). Adolescents'

experiences of HIV are typically characterized by isolation, stigma and shame, which impede their adherence (Enane et al., 2020; Bernays et al., 2017). They are concerned to protect social relationships by concealing their HIV status and use of ART (Kawuma et al., 2014).

Many caregivers, and sometimes healthcare workers, actively discourage ALWH from disclosing their status, thereby cutting them off from potential sources of support (Mackworth-Young et al., 2017). Disclosure of HIV status may pose substantial risks for adolescents and damage social relationships (Mackworth-Young et al., 2017), with subsequent negative effects on adherence and mental health (MacCarthy et al., 2018).Disclosure has been shown to be a protective factor as far as viral suppression is concerned. This could be due to the association between disclosure of HIV status and adherence. Some studies have found delayed or nondisclosure of HIV status to be associated with virological failure (Abadia-Barrero and Larusso, 2006). Attention should be focused on increased involvement of the adolescent and family in medical treatment after disclosure.

Disclosed adolescents have better access to social support and tend to be less depressed over the long-term, thereby adhering to their medication well (Abadia-Barrero and Larusso, 2006).Those who were on first line treatment were less likely to develop virological non-suppression as compared to those on second line treatment regimen. This finding agrees with a study conducted in Zimbabwe on virologic non-suppression among adolescents living with HIV which revealed that adolescents on first line are less likely to develop virologic non-suppression (Sithole et al., 2018).

In this study, there was no significant association between gender and virologic non-suppression. On the contrary, some studies have reported that males had increased odds of virological non-suppression (Kadima et al., 2018), whilst other studies however found no association between gender and virological non-suppression (Jobanputra et al., 2015). The role of gender in virological suppression could be biologic (Fokam et al., 2017). Additionally, a systematic review of adolescent

ART adherence in low and middle-income countries (8/15 studies from sub-Saharan Africa) found no consistent association between virologic non-suppression and gender (Hudelson et al., 2015). The relationship of virological suppression and gender is therefore inconclusive and requires further studies.

This study revealed that there was no significant association between age and virologic non-suppression among HIV positive adolescents. Similarly, a retrospective study in Kenya (Mwangi, 2019) and a prospective cohort study in Tanzania (Muri et al., 2017) found no association between virologic non-suppression and age.This study found no statistically significant relationship between education level and virologic non-suppression. This agrees with a Danish HIV Cohort reported by Legarth et al., (2014) which also showed no association between education level and virological non-suppression.

Clinical factors associated with viral load non-suppression among HIV infected adolescents.

Having a comorbidity, such as tuberculosis in most of the cases, increased the odds of being virally non-suppressed. These findings are in line with a study inZimbabwe and in South Africa, which showed that adolescents on prolonged medication for another disease were likelier to be virally non-suppressed (Sithole et al., 2018).This study found that having a history of previous TB treatment increased the odds of having virological non-suppression by as much as five times. These findings agree with studies reported by Ahoua et al., (2009), and by Rajin et al., (2017). On the other hand, it has been recently reported that children who had a history of TB co-infection had better virological outcomes (Kadima et al., 2018).

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 study could be due to the increased pill burden and drug-

drug interactions between the medications for TB and HIV therapies, especially the NNRTIs or PIs in the setting of rifampin-containing TB treatment. The significance of TB comorbidity on the occurrence of virological non-suppression buttresses the need for the prioritization of frequent viral load monitoring and adherence support in TB/ HIV co-infected patients as well as patients who have a history of previous TB. While this study was not able to examine the effect of other opportunistic infections (OIs), it is important to note that non-TB opportunistic infections are now less common than in the past because of early HIV diagnosis and initiation of effective ART. As a result, there is reduction of OI-related morbidity and mortality in person with HIV (Goldschmidt et al., 2016).

Studies on the relationship between self-reported adherence to ART and virological non- suppression have shown inconsistent results (Nieuwkerk and Oort, 2005). 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., (2014), in Cambodian adolescents, non-adherence was associated with virological non-suppression. The measure of adherence used in the study by Intasan et al., (2014), was however the 3-day self -report by caregiver. In more recent research by Natukunda et al., (2019), in adolescents, more than 70% of adolescents who experienced virological non-suppression were sufficiently adherent as measured by pill count (adherence > 95%). Also, this study found no association between WHO stage and virologic non-suppression among adolescents living with HIV. Similarly, other studies revealed that WHO stage was not associated with virological failure (Hailu et al., 2018; Bayu et al., 2017).

Conclusion

In conclusion, this study found that adolescents continue to face worse HIV viral load outcomes. The determinants of viral load non-suppression among adolescents are unique and thus require unique interventions. Urgent adolescent-friendly strategies to decrease non-suppression rates such a peer involvement, viral load focal persons to identify viral load non-suppression and actively follow up

with these adolescents, patient education on viral load non-suppression, and demand creation for ART especially for newly initiated adolescents and adolescents on ART for protracted periods, should be laid with these determinants in mind so that they (strategies) are targeted, if efforts to achieve HIV epidemic control in resource-limited settings are to be successful.

Recommendations

While adhering to confidentiality, program counsellors should work with adolescents, their close family members to ensure successful positive serostatus disclosure; ART related Services at the facility should be adolescent friendly through age specific triaging and provision of privacy; ART programs should develop social and economic support system for adolescents that include family members and well-wishers to prevent treatment failure; and the need to monitor suppression by age group to understand different needs and challenges that affect suppression

Supervision and monitoring the healthcare workers especially counsellors to document session proceedings such that treatment plans can be developed for those in need of intensive adherence counselling**;** conducting mass sensitization about importance of adherence, family support for HIV positive adolescents on ART**; v**iral load testing should be made accessible to all adolescents through an effective referral system, increasing number of health facilities with viral load testing equipment and trained personnel; and adolescent clients should be managed based on clinical care such CD4 count and WHO clinical staging

Abbreviations

AIDS: Acquired Immuno-Deficiency Syndrome, **ART:** Antiretroviral therapy, **CD4:** Cluster of Differentiation 4, **HC:** Health Centre, **HCT:** HIV counseling and testing, **HIV:** Human Immunological Virus, **LFTU:** Lost to Follow Up, **MCC:** Mbarara City Council, **NVP:** Nevirapine, **PLWHIV:** People Living With HIV, **RNA:** Ribonucleic acid, **SSA:** Sub Saharan Africa, **USAID:** United States Agency for International Development, **VLNS:** Viral load non-suppression, **WHO:** World Health Organization, **ARV:**Antiretroviral, **VLNA:** Viral load non-suppression, **ART:**

Antiretroviral therapy, **UNICEF:** United Nations International Children's Emergency Fund, **UNAIDS:** United Nations AIDS Program.

Availability of data and materials

The datasets used and/or analyzed for this study are available from the corresponding author upon reasonable request.

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Declarations

Acknowledgement

The authors would like to thank the leadership of the city for allowing this study to be conducted in Mbarara City; we also thank the adolescents and healthcare facility staff who participated in the study. Special thanks go to the research assistants that were pivot in interviewing andcollecting the data.

Funding

Not applicable

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Contributions
JN, IA, RL and TM conceived and designed the study: JN implemented the study: IA and RL supervised the study: JN and TM conducted data analysis: JN, IA, RL and TM interpreted study results: JNand TMwrote the first draft of the manuscript, while IA andRL reviewed and corrected the manuscript. All authors read and approved the final manuscript.

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Ethical declarations
Ethics approval and consent to participate
The Institutional Review Board of The Aids Support Organization (TASO) approved the study (). The respondents recruited to participate in the study, were explained to the purpose, process and expectation of the study.

All participants were assured of maximum confidentiality with which data collected would be treated. Withdrawal from the study at any time the respondent wished was accepted. Informed consent was obtained from all respondents aged 18-19 years while those of ages 14-17 years were considered as mature minor as described by Uganda National Council of Science and Technology and assented. Adolescents aged 10-13 years assent was obtained from themand consent wasalso be obtained from their caretakers.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests

Figure 1 showing the proportion of adolescents with non-suppressed viral load

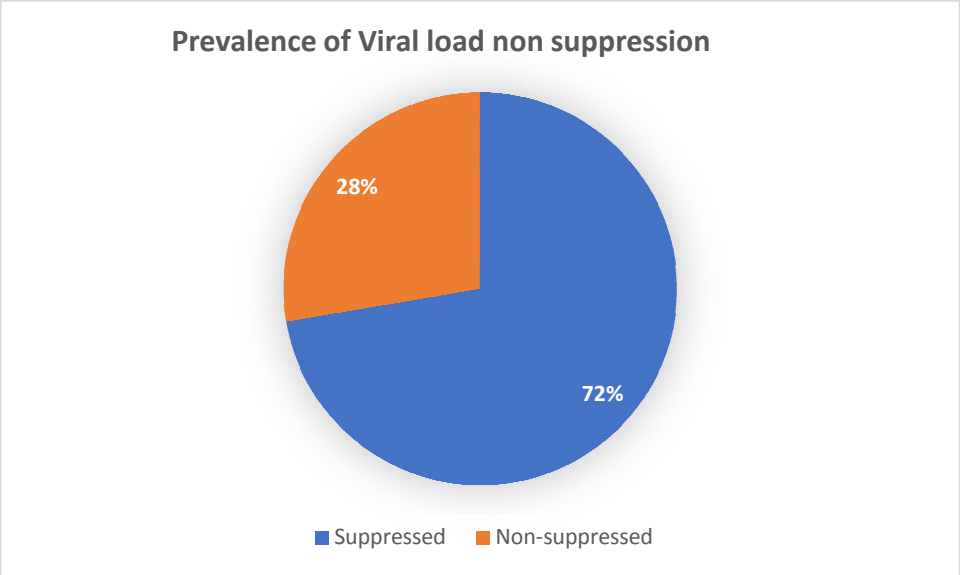

Table 1. The number of adolescents to be interviewed at each health facility was determined using the proportionate sampling.

No.	Name of Facility	No. of active Adolescent in HIV care by end of December 2019 (a)	Proportionate Sample from each site. (x)= (a/502*303)
1	Mbarara Municipal Council HC IV	156	94
2	Kakoba HC III	12	7
3	TASO Mbarara Clinic	226	136
4	Nyamitanga HC III	10	6
5	Nyakayojo HC III	14	8
6	Biharwe HC III	26	16
7	Nyamityobora HCII	7	4
8	Ruti HC II	14	8
09	Holly Innocents Hospital	5	3
10	Ruharo Mission Hospital	14	8
11	Mbarara Community Hospital	5	3
12	Kamukuzi Division HCII	4	2
13	AIDS Information Centre	5	3
114	Mayanja Memorial Hospital	4	2
	Total	**502**	**302**

Table 2: virological non-suppression of adolescents on ART stratified by socio-demographic and clinical characteristics.

Characteristics		Suppression status		χ^2	P-Values
		Yes	No		
Age	10-14	98 (74.24%)	34 (25.76%)	0.429	0.512
	15-19	119 (70.83%)	49 (29.17%)		
Gender	Male	76 (71.03%)	31 (28.97%)	0.142	0.707
	Female	141 (73.06%)	52 (26.94%)		
Level of education	None	9 (100.00%)	0 (0.00%)		
	Primary	123 (93.89%)	8 (6.11%)	0.887	0.642
	Secondary	148 (92.50%)	12 (7.50%)		
Religion	Catholic	35 (74.47%)	12 (25.53%)		
	Protestant	121 (69.94%)	52 (30.06%)		
	Moslem	35 (85.37%)	6 (14.63%)	5.619	0.230
	Pentecost	14 (73.68%)	5 (26.32%)		
	SDA	12 (60.00%)	8 (40.00%)		
Family support	Parent(s)	60 (81.08%)	14 (18.92%)		
	Guardian	126 (71.59%)	50 (28.41%)		
	Peer	11 (78.57%)	3 (21.43%)	8.658	0.070
	Matron/school nurse	4 (66.67%)	2 (33.33%)		
	Relative	16 (53.33%)	14 (46.67%)		
Belong to an adolescent group	Yes	37 (80.43%)	9 (19.57%)		
	No	180 (70.87%)	74 (29.13%)	1.782	0.182
Parents alive	Yes	133 (78.70%)	36 (21.30%)	7.835	**0.005****
	No	84 (64.12%)	47 (35.88%)		
Caregiver HIV status	Negative	9 (56.25%)	7(43.75%)		
	Positive	70 (78.65%)	19 (21.35%)	4.082	0.130
	I don't know	138 (70.77%)	57 (29.23%)		
HIV status disclosure	Yes	139 (78.53%)	38 (21.47%)	8.286	**0.004****
	No	78 (63.41%)	45 (36.59%)		
Distance from health facility	< 2 km	14 (100.00%)	0 (0.00%)		
	2 – 5 km	203 (93.98%)	13 (6.02%)	2.396	0.302
	> 5 km	63 (90.00%)	7 (10.00%)		
WHO stage at ART initiation	1 and 2	187 (71.37%)	75 (28.63%)		
	3 and 4	30 (78.95%)	8 (21.05%)	0.951	0.329
Ever had active TB in last 12 months	Yes	0 (0.00%)	20 (100.00%)		
	No	217 (77.50%)	63 (22.50%)	56.024	**0.000*****
Duration on ART	1 – 2 years	19 (79.17%)	2 (8.33%)		
	2 - <5 years	39 (68.42%)	18 (31.58%)	1.004	0.605
	> 5 years	159 (72.60%)	60 (27.40%)		
ART line at initiation	1st line	212 (77.37%)	62 (22.63%)	40.113	**0.000*****
	2nd line	5 (19.23%)	21 (80.77%)		

Current ART regimen	EFV based	38 (63.33%)	22 (36.67%)		
	DTG based	117 (75.48%)	38 (24.52%)	3.491	0.322
	NVP based	17 (77.27%)	5 (22.73%)		
	LPV/r based	45 (71.43%)	18 (28.57%)		
Level of adherence	Good >95%	207 (76.95%)	62 (23.05%)		
	Fair 85 – 94%	10 (90.91%)	1 (9.09%)	57.053	**0.000*** **
	Poor <85%	0 (0.00%)	20 (100.00%)		

Table 2: Correlates of viral load non-suppression

Factors	Viral load suppression status		Crude OR (95% CI)	Adjusted OR (95% CI)
	Yes	No		
ART initiation line				
2nd line	5 (19.23%)	21 (80.77%)	1	1
1st line	212 (77.37%)	62 (22.63%)	14.36 [5.20 39.65] ***	10.90 [3.79 31.41] ***
Belong to an adolescent group				
No	180 (70.87%)	74 (29.13%)	1	
Yes	37 (80.43%)	9 (19.57%)	1.69 [.78 3.68]	
Family support				
Relative	16 (53.33%)	14 (46.67%)	1	
Parent(s)	60 (81.08%)	14 (18.92%)	3.75 [1.49 9.44] **	
Guardian	126 (71.59%)	50 (28.41%)	2.21 [1.00 4.85] *	
Friend	11 (78.57%)	3 (21.43%)	3.21 [.74 13.87]	
Matron	4 (66.67%)	2 (33.33%)	1.75 [.28 11.05]	
Parents alive				
No	84 (64.12%)	47 (35.88%)	1	1
Yes	133 (78.70%)	36 (21.30%)	2.07 [1.24 3.45]	1.474 [1.01 3.02] *
Caregiver HIV status				
Don't know	138 (70.77%)	57 (29.23%)	1	
Negative	9 (56.25%)	7 (43.75%)	.53 [.19 1.49]	
Positive	70 (78.65%)	19 (21.35%)	1.52 [.84 2.75]	
Disclosure				
No	78 (63.41%)	45 (36.59%)	1	1
Yes	139 (78.53%)	38 (21.47%)	2.11 [1.26 3.53]	1.20
Adherence level				
Poor	0 (0.00%)	20 (100.00%)	1	
Fair	207 (76.95%)	62 (23.05%)	2.23 [.49 9.99]	
Good	10 (90.91%)	1 (9.09%)	6.200 [2.37 16.22]	.32

