Viral suppression and associated factors among children tested for HIV viral load at Amhara Public Health Institute, Dessie Branch, Ethiopia: a cross-sectional study

Hailu Berihun, Getaw Walle Bazie, Altaseb Beyene, Amare Zewdie

ABSTRACT

Objective This study aims to assess viral suppression and associated factors among children tested for HIV viral load at the Amhara Public Health Institute, Dessie Branch, Ethiopia.

Design An institutional cross-sectional study was conducted. An observational checklist was used to collect the data. Data were entered into EpiData and analysed using SPSS (V.25). The data were analysed descriptively. Variables with p=0.25 from the bivariable analysis were entered into a multivariable logistic regression model, and significant variables (p=0.05) were retained in the multivariable model.

Setting and participants This cross-sectional study was conducted among 522 randomly selected children tested for HIV viral load at the Amhara Public Health Institute, Dessie Branch, Ethiopia. The study included children under the age of 15 years with complete records.

Results Viral suppression was 73% (95% CI: 60.41% to 77.63%). Treatment duration on antiretroviral therapy (adjusted OR (AOR)=0.207; 95% CI: 0.094 to 0.456) and regimen substitution (AOR=0.490; 95% CI: 0.306 to 0.784) were significantly associated with viral suppression rate.

Conclusions In this study, the overall magnitude of viral suppression in Amhara Public Health Institute, Dessie Branch is low as compared with the WHO’s 95% viral suppression target. Viral suppression was significantly associated with antiretroviral therapy duration and regimen substitution.

INTRODUCTION

Virological non-suppression occurs due to a history of tuberculosis (TB) treatment, female gender and severe CD4 immune suppression (CD4\% 15%/CD4+ count 200 cells/mm³) at the time of recruitment and while on a nevirapine (NVP)-based regimen. The proportion of HIV-positive adolescents on antiretroviral therapy (ART) who were not virologically suppressed after 6 months was 23% in South Africa. WHO stage IV and ART-related facial outcomes were strongly associated with virological non-suppression, whereas an earlier age of onset of 5 years or more was considered protective compared with WHO stage I. In Eswatini, HIV-positive children on ART and on antiretroviral drug regimen experienced viral suppression at a rate of 77.9%, with NVP-based ART having the lowest rates. After 1–5 years on highly active ART (HAART), more than half of Nigerian children receiving HAART had a viral load above 1000 copies/mL. Prolonged ART duration and use of zidovudine, lamivudine and NVP were associated with viral loads >1000 copies/mL. Poor adherence and viral resistance must be considered.

Poorly controlled HIV can be due to many factors, including poor health, poor medication adherence, drug resistance and drug toxicity. According to the WHO, children represent a very vulnerable population: one in two children newly diagnosed with HIV infection have virus resistance to both efavirenz (EFV) and NVP; therefore, there is a high risk of suboptimal treatment.

In Northwest Ethiopia, higher virological failure and lower viral suppression rates...
among children receiving ART were seen among those experiencing ART than those not experiencing it.\textsuperscript{7} Patients with poor adherence and WHO stage II status were significantly associated with viral infection not being suppressed in men.\textsuperscript{8} Compared with adult HIV infection, paediatric HIV infection has received less research attention and funding over the past decades, which is why paediatric HIV infection is considered a neglected disease.\textsuperscript{9} Virological failure has been associated with rapid progression to AIDS, which impacts the patient’s health and economy by increasing hospital readmissions and increasing health costs by making clients repeatedly visit health facilities and losing economic benefits. Treatment combination, history of TB treatment, being on second-line and third-line regimens, time on ART, CD4 immune suppression, WHO staging and demographic factors all contribute to treatment failure. It is thus important to recommend age-specific interventions, especially for children under 5 years of age, to improve virological suppression in HIV-positive adolescents receiving ART in this setting.\textsuperscript{6} The best possible care for children who are not cured must be provided.\textsuperscript{7} The guidelines highlight the importance of monitoring treatment programmes to optimise paediatric HIV cure.\textsuperscript{5} In this context, describing the magnitude of viral suppression rates and elucidating the causes of viral suppression may help to address the pressing need to find interventions to maximise viral suppression among young people on ART and achieve international HIV goals by minimising regimen switches, thereby improving current practices and preventing the emergence and spread of new viral strains.

Regular monitoring and assessment of viral suppression are important to achieve established goals and take necessary corrective actions. A single study done in Bahir Dar cannot inform policymakers as comprehensively as the Ethiopian data. Furthermore, no documented information about viral suppression and factors is available at the Amhara Public Health Institute, Dessie Branch, Ethiopia. It also filled the gap well in the study area. Therefore, this study aims to assess the viral suppression and associated factors among children tested for HIV viral load at the Amhara Public Health Institute, Dessie Branch, Ethiopia.

**MATERIALS AND METHODS**

**Study design and period**

An institution-based cross-sectional study design was conducted from March to June 2022.

**Population**

All children less than 15 years of age receiving HIV viral load testing services at the Amhara Institute of Public Health, Dessie Branch were used as the source population. Participants less than 15 years tested for viral load from March to June during the data collection period were considered as the study population. Fully recruited children under the age of 15 years were included in the study.

**Sampling method and sample size determination**

The sample size was determined by using a single proportion formula by taking the following assumptions: prevalence from a previous study conducted at Amhara Public Health Institute, Bahir Dar (72%)\textsuperscript{6} with a 95% CI, 5% marginal error and 10% non-response rate.

\[
N = \left(1.96\right)^2 \left(0.72\right) \left(1 - 0.72\right) = 309
\]

Finally, by adding 10% non-response rate, the total sample size was 340.

**Sample size determination for the second objective**

The sample size for the factor associated with viral suppression among children obtained from literature is calculated by EpInfo V.7, by considering the following assumptions: confidence level 95%, power 80% and exposure-to-unexposed ratio of 1. The detailed summary of sample size calculation for this objective is shown in table 1 below.

Finally, the sample sizes were calculated for the first and second objectives, and the largest sample size is 522 from both the first and second objectives after adding a non-response rate (10%).

The laboratory receptionist prepared a list of all eligible participants aged 15 years old receiving ART for viral load testing at the Amhara Institute of Public Health, Dessie Branch in 2022. Once eligible children were identified, the desired sample size was selected by simple random sampling. A lottery procedure was used to select the 522 samples accepted. Each member of the population was assigned a sampling code, and numbers are chosen at random.

**Operational definitions**

Adherence to ART is taking one’s medicine as prescribed and agreed upon between the patient and provider, which is 95% or more adherence to ART (missing ≤2 doses of 30

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**Table 1** Sample size for the factors associated with viral suppression

<table>
<thead>
<tr>
<th>Factors associated with viral suppression</th>
<th>% outcome among unexposed</th>
<th>AOR (95% CI)</th>
<th>Total sample size</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nevirapine-based ART</td>
<td>68.9</td>
<td>1.95 (1.45 to 2.63)</td>
<td>418</td>
<td>\textsuperscript{6}</td>
</tr>
<tr>
<td>Poor adherence</td>
<td>57.1</td>
<td>1.905 (0.80 to 4.55)</td>
<td>362</td>
<td>\textsuperscript{6}</td>
</tr>
<tr>
<td>PI-based ART</td>
<td>69.5</td>
<td>1.81 (0.71 to 4.60)</td>
<td>522</td>
<td>\textsuperscript{6}</td>
</tr>
</tbody>
</table>

AOR, adjusted OR; ART, antiretroviral therapy; PI, protease inhibitor.
doses or ≤3 doses of 60 doses) and adherence to treatment information given by the physician.\textsuperscript{10} Non-adherence to ART is the condition of missing doses completely, not following information given by the physician, as well as taking drugs inappropriately (less than 95% adherence=2 doses of 30 doses or ≥3 doses of 60 doses), and not adherent to treatment information given by the physician.\textsuperscript{10}

Good adherence refers to >95% adherence; fair refers to 80%–95%, while poor adherence is less than 80%.\textsuperscript{11} Viral suppression and failure are determined using the WHO definitions (viral suppression as viral load <1000 copies/mL and virological failure ≥1000 copies/mL).\textsuperscript{12} According to the US Centers for Disease Control and Prevention, undetectable viral load means <200 copies/mL.\textsuperscript{12}

Detectable viral load considers a level of viral load that is too low to be picked up by the particular viral load test being used or below an agreed threshold (such as 50 copies/mL or 200 copies/mL).\textsuperscript{13} Primary healthcare level (health post, health centre and primary hospital), secondary healthcare level (general hospital) and tertiary level (specialised hospital).\textsuperscript{14}

**Data collection procedure**

An observational checklist was used to assess viral suppression among children tested in the Amhara Public Health Institute, Dessie Branch. The data collection tool was prepared by the investigator and used to collect data. Samples at the central reception of the Amhara Public Health Institute, Dessie Branch were checked for completeness of requests. The lower and higher detection limits of the PCR machine are 150 and 10,000,000 RNA copies/mL, respectively. Results with greater than 1000 HIV RNA copies/mL extracted from semen were considered as not suppressed viral load results.

**Data quality assurance**

After the pretest, the necessary amendment was made. One day of training was given to the data collectors and supervisors on the questionnaire and data collection process. The data collectors were trained on assessment and data collection procedures by a researcher in an institute before starting data collection. All checklists were checked daily to ensure that they were appropriately filled. Any missing data were confirmed before the next day’s checklist review. In addition, the quality of data collection was ensured through the daily close supervision of the data collection team by the principal investigator. A supervisor closely followed up on the data collection activities, ensuring complete and ethical data collection. At the end of the data collection, double data entry was conducted to check the consistency.

**Data processing and analysis**

Data were checked for completeness and consistency, after which it was coded and entered into EpiData V.4.6.0.2, and then exported to SPSS V.25 statistical software for processing and analysis. Different frequency tables, graphs and descriptive summaries were used to describe the study variables. Logistic regression analysis was used to see the significance of the association between dependent and independent variables. Bivariable and multivariable analyses were used to see the association between viral suppression rate and selected independent variables. In bivariable logistic regression analysis, a variable with a p value of 0.25 or less was entered for multivariable logistic regression analysis, and an adjusted OR with 95% CI was calculated to identify strength and significance of the association. The adequacy of the final model was checked using the Hosmer-Lemeshow goodness-of-fit test.

**Patient and public involvement**

There was no direct interaction with patients in this study and no direct patient involvement in the design or conduct of this study.

**RESULTS**

**Sociodemographic characteristics of participants**

A complete data set was obtained from 522 children aged 15 years who were tested for viral load, which gave a response rate of 100%. Three hundred nineteen (61.1%) were girls, and 394 (75.5%) were over the age of 10 years. Four hundred twenty-three (81%) of the respondents lived in rural residences. About 336 (64.4%) of the children were from South Wollo (table 2).

**Viral suppression**

Out of 522 children, 379 (73%) (95% CI: 60.41 to 77.63) had suppressed viral loads.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Categories</th>
<th>Frequency</th>
<th>Per cent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>&lt;5</td>
<td>19</td>
<td>3.6</td>
</tr>
<tr>
<td></td>
<td>5–9</td>
<td>109</td>
<td>20.9</td>
</tr>
<tr>
<td></td>
<td>+10</td>
<td>394</td>
<td>75.5</td>
</tr>
<tr>
<td>Sex</td>
<td>Male</td>
<td>203</td>
<td>38.9</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>319</td>
<td>61.1</td>
</tr>
<tr>
<td>Place of residence</td>
<td>Urban</td>
<td>99</td>
<td>19.0</td>
</tr>
<tr>
<td></td>
<td>Rural</td>
<td>423</td>
<td>81.0</td>
</tr>
<tr>
<td>Zone</td>
<td>South Wollo</td>
<td>336</td>
<td>64.4</td>
</tr>
<tr>
<td></td>
<td>North Wollo</td>
<td>166</td>
<td>31.8</td>
</tr>
<tr>
<td></td>
<td>Oromia</td>
<td>13</td>
<td>2.5</td>
</tr>
<tr>
<td></td>
<td>Special Zone</td>
<td>7</td>
<td>1.3</td>
</tr>
</tbody>
</table>

Table 2 Sociodemographic characteristics of HIV-infected children tested for viral load at Amhara Public Health Institute, Dessie Branch from March to June 2022.
Clinical characteristics of HIV-infected children

The study found that 491 (94.1%) of the children were in WHO stage I. The children were treated using EFV-based (69; 13.2%), NVP-based (31; 5.9%), protease inhibitor-based (19; 3.6%) and integrase inhibitor-based (403; 77.2%) antiretroviral drugs. In terms of ART duration, 30 (5.7%) of study participants had been on treatment for less than 12 months, 170 (32.6%) had been on treatment for between 12 and 48 months, and 322 (61.7%) had been on treatment for more than 48 months. For viral load testing, the goal was to confirm virological treatment failure in 12 (2.3%) suspects and routine viral load in 510 (97.7%) HIV-infected children (table 3).

Associated factors of viral load suppression

In the bivariable binary logistic regression, four variables, including the duration of ART, history of TB treatment, history of regimen substitution and current regimen status, were candidates for inclusion in the multivariable analysis. The odds of having viral suppression among patients who had been on ART for less than 12 months were 57.9% lower compared with the odds of having viral suppression among patients on ART for the duration of 48 months and more (adjusted OR (AOR) 0.207 (95% CI: 0.094 to 0.456). The odds of having viral suppression among patients who substituted their regimen were lower compared with the odds of having viral suppression among patients with no regimen substitution (AOR 0.490; 95% CI: 0.306 to 0.784) (table 4).

DISCUSSION

This study examined the rate of viral load suppression in children tested at the Amhara Public Health Institute, Dessie Branch. The overall magnitude of viral suppression in the study area was 73% (95% CI: 60.41% to 77.63%), falling far short of the WHO’s target of 95% by 2025. In a previous study, similar results were found, showing 61.6% had virological suppression in southern Ghana. In Nigeria, approximately 70% of children were found to be virally infected but not suppressed. Similarly, in Bahir Dar, Ethiopia, 71% of the HIV viral load was suppressed. But in the current study, there was a higher viral suppression rate than in the study conducted in southern Ghana and Niger. The difference might be due to differences in the study design, study area and so on.
methods used to measure viral suppression rate, as well as the sociodemographic characteristics of the study participants. Unsuppressed viral load in patients on ART happens when treatment fails to suppress a patient’s viral load, the CD4 count goes down and the immune system weakens, and is associated with reduced survival and elevated transmission. Another possible explanation for the difference might be that this emphasises the need for accurate tracking and appropriate management of children receiving ART to suppress this viral load, which was higher in our study area. In May, an emergency centre was established in the Amhara region to assist with the high HIV viral load.

Treatment duration of ART less than 12 months (AOR 0.207 (95% CI: 0.094 to 0.456)) showed significantly lower viral suppression compared with treatment duration greater than 48 months. This is in line with a retrospective study conducted in Ghana, which found that being on ART for more than 3 years was a factor associated with achieving viral suppression. In this study, the odds of low viral suppression were more likely among HIV-infected children on ART with duration of ART greater than 4 years and who substituted their regimen compared with their counterparts. The possible reason might be attributed to a lack of follow-up and comprehensive monitoring of HIV-infected children. It stresses the need for close monitoring and proper management of children on ART in this study setting with the collaboration of referring health facilities to suppress their viral loads.

CONCLUSION
In this study, the overall magnitude of the viral suppression rate in the Amhara Public Health Institute, Dessie Branch was low in comparison with the WHO’s target for viral suppression. Duration of ART and regimen substitution are significantly associated with viral suppression. The managing bodies of health facilities should strive to plan, monitor and evaluate HIV programme services, especially for those HIV-infected children with poor adherence, by including them in health education sessions, morning sessions and meeting agendas.

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Contributors Conceptualisation—HB, GWB and NK. Investigation—HB. Methodology—HB, GWB, AB and NK. Formal analysis and software—HB, GWB, AB, AZ and NK. Writing (original draft)—GWB, AB, AZ and NK.

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Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not required.

Ethics approval Ethical approval was obtained from the research and ethical review committee of Zemen Postgraduate College of Health Science (ref no: CMHS/85/14/2022). Permission was obtained from the Amhara Public Health Institute, Dessie Branch (APHIDB). Written informed consent was obtained from laboratory reception before the data collection process. The information was gathered from the laboratory request, the Excel database and the results of the specimens referred to the APHIDB reference laboratory. Data collectors were professionals working in the respective laboratories who knew the national guidelines on HIV/AIDS. Data were collected anonymously and personal information was stored securely in locked file cabinets when not in use and handled only by trained staff members when actively used during research. All collected data were used for research purposes. All methods and materials were performed according to the guideline.

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