BRIEF REPORT

Children and adolescents on anti-retroviral therapy in Bulawayo, Zimbabwe: How many are virally suppressed by month six? [version 1; peer review: 2 approved, 1 approved with reservations]

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Abstract

Background: Zimbabwe is one of the countries in sub-Saharan Africa disproportionately affected by human immunodeficiency virus. In the “treat all” era, we assessed the gaps in routine viral load (VL) monitoring at six months for children (0-9 years) and adolescents (10-19 years) newly initiated on anti-retroviral therapy (ART) from January 2017 to September 2018 at a large tertiary hospital in Bulawayo.

Methods: In this cohort study using secondary data, we considered first VL done within six to nine months of starting therapy as ‘undergoing VL test at six months’. We classified repeat VL ≥ 1000 copies/ml despite enhanced adherence counselling as virally unsuppressed.

Results: Of 295 patients initiated on ART, 196 (66%) were children and 99 (34%) adolescents. A total 244 (83%) underwent VL test at six months, with 161 (54%) virally suppressed, 52 (18%) unsuppressed and 82 (28%) with unknown status (due to losses in the cascade). Switch to second line was seen in 35% (18/52). When compared to children, adolescents were less likely to undergo a VL test at six months (73% versus 88%, p=0.002) and more likely to have an unknown VL status (40% versus 22%, p=0.001).

Conclusion: At six months of ART, viral suppression was low and losses in the cascade high.
Keywords
Children living with HIV, Adolescent living with HIV, EAC, Mpilo, Operational research, SORT IT

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Author roles: Moyo S: Conceptualization, Data Curation, Formal Analysis, Methodology, Visualization, Writing – Original Draft Preparation, Writing – Review & Editing; Ncube RT: Conceptualization, Formal Analysis, Methodology, Software, Visualization, Writing – Original Draft Preparation, Writing – Review & Editing; Shewade HD: Conceptualization, Formal Analysis, Methodology, Software, Visualization, Writing – Original Draft Preparation, Writing – Review & Editing; Ngwenya S: Conceptualization, Methodology, Writing – Review & Editing; Takarinda KC: Data Curation, Writing – Review & Editing; Dzangare J: Data Curation, Writing – Review & Editing; Goverwa-Sibanda TP: Data Curation, Writing – Review & Editing; Apollo T: Conceptualization, Methodology, Project Administration, Supervision, Writing – Review & Editing

Competing interests: No competing interests were disclosed.

Grant information: This research was conducted through the Structured Operational Research and Training Initiative (SORT IT), a global partnership led by the Special Programme for Research and Training in Tropical Diseases at the World Health Organization (WHO/TDR). The training model is based on a course developed jointly by the International Union Against Tuberculosis and Lung Disease (The Union) and Médecins sans Frontières (MSF). The specific SORT IT program which resulted in this publication was implemented by the Centre for Operational Research, The Union, Paris, France. Mentorship and the coordination/facilitation of this particular SORT IT workshop was provided through the Centre for Operational Research, The Union, Paris, France; the Department of Tuberculosis and HIV, The Union, Paris, France; The Union, Zimbabwe Office; The Union, South East Asia Office; and AIDS & TB Department, Ministry of Health & Child Care, Harare, Zimbabwe. The training course under which this study was conducted was funded by: the United Kingdom’s Department for International Development (DFID); and the World Health Organization Zimbabwe Country Office.

The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

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How to cite this article: Moyo S, Ncube RT, Shewade HD et al. Children and adolescents on anti-retroviral therapy in Bulawayo, Zimbabwe: How many are virally suppressed by month six? [version 1; peer review: 2 approved, 1 approved with reservations]
Introduction

In 2014, the Joint United Nations Programme HIV/AIDS (UNAIDS) announced ambitious new global 90-90-90 fast-track HIV targets for 2020. These targets were further supported by the 2016 “treat-all” WHO recommendations. With the expansion of anti-retroviral treatment (ART) coverage, investments in the global response are shifting towards sustained viral suppression for improved survival and epidemic control. This is in the context of scaling up viral load (VL) monitoring to ensure 90% of people in care are virally suppressed (VL<1000 copies per ml). Globally in 2018, only 918 000 (54%) children aged 0–14 years living with HIV received ART. HIV is among the top 10 leading causes of death among adolescents, a period where sustained adherence is particularly challenging, the only age group where deaths from HIV has not decreased.

Zimbabwe is disproportionately affected by HIV. In 2017, 1.4 million people were living with HIV, with 5.8% being children 0–14 years. An estimated 15% on ART have high VL. The national ART guidelines recommend routine VL monitoring at six and 12 months, and then annually if stable on ART. The extent to which routine VL monitoring is being implemented specifically for children and adolescents in the “treat-all” era has not been explored in Zimbabwe. We therefore assessed the gaps in routine VL monitoring at six months for children (0–9 years) and adolescents (10–19 years) initiated on ART at a large tertiary hospital in Bulawayo, Zimbabwe.

Methods

Study design

We conducted a cohort study involving secondary data.

Setting

Mpilo Opportunistic Infections (OI) Clinic is within Mpilo Central Hospital in Bulawayo (the second largest city in Zimbabwe). It is a tertiary facility, managing complicated referrals, including patients on second and third line treatment. VL testing is offered as per national guidelines at the hospital HIV laboratory, adjacent to the clinic. Patient data are routinely entered in the electronic point of care database, ART register and patient care booklet.

First line ART regimen for children <3 years is ABC+3TC+LPV/R or AZT+3TC+LPV/r. Children 3–9 years and adolescents <35kg receive AZT+3TC+NVP or ABC+3TC+EFV, while adolescents >35kg receive TDF+3TC+NVP or EFV. Those with VL ≥1000 copies/ml at six-months are offered enhanced adherence counseling (EAC), and a second VL test after three months. A repeat VL ≥1000 copies/ml (despite EAC) is classified as virally unsuppressed, and eligible for second line ART.

Study population

We included all children (0–9 years) and adolescents (10–19 years) newly initiated on first line ART at Mpilo OI Clinic between January 2017 and September 2018.

Data extraction and analysis

We extracted anonymized patient data from electronic patient and laboratory databases, analyzed using STATA (version12.1 STATA Corp., College Station, TX, USA). If data were missing in electronic databases, we referred to paper-based registers and booklets. We defined low CD4 count as follows: CD4 count ≤350 cells/mm³ for children and adolescents >5 years, and CD4% <25% of total lymphocytes for children <5 years. We defined ‘undergoing VL testing at six months’ as those with first VL tests done within six to nine months of starting ART. Comparisons were made between children and adolescents using chi squared test.

Ethics

We received ethics approval from Medical Research Council of Zimbabwe (MRCZ E/248), The Union Ethics Advisory Group, Paris, France (EAG 52/19) and the Mpilo Hospital Ethics Board. As the study involved review of secondary data, the ethics committee(s) waived the need for written informed consent.

Results

Of 295 patients initiated on ART during the study period, 196 (66%) were children and 99 (34%) adolescents. A total 141 (48%) were boys, 209 (71%) were WHO stage I or II, and 119 (40%) had severe anemia. Baseline CD4 count was available for 188, among whom 94 (50%) had low CD4 cell count.

Of 295, a total of 244 (83%) underwent VL test at six months, which was significantly lower among adolescents when compared to children (73% versus 88%, p=0.002) (Figure 1). Of 295, 52 (18%) were virally unsuppressed, 161 (54%) virally suppressed and 82 (28%) unknown (unknown due to loss to follow up after ART initiation). Unsuppressed VL was not different among children and adolescents, though unknown VL suppression status, was higher among adolescents (40% versus 22%, p=0.001) (Table 1). Switch to second line was among 18 out of 52 eligible (35%), with no significant difference between adolescents and children (21% versus 39%, p=0.376) (Figure 1).

Discussion

This is one of the first studies from Zimbabwe attempting to assess the extent to which routine VL monitoring at six months is being implemented, specifically for children and adolescents in the “treat-all” era.

Overall, one in five of those initiated on ART were virally unsuppressed at six months. The true estimate could be higher considering viral suppression was unknown for one-third of children. High unsuppressed VL and the observed attrition along the care cascade, undermines the last ‘90’ of the UNAIDS 90-90-90 targets in this special sub-population. This study, adolescents were more likely to be lost in the cascade compared to children, calling for focussed interventions for this sub-group. This is despite of a comprehensive adolescent ART
program at the clinic, and suggests a reversal of gains made earlier in the program.⁹

Compared to findings in Harare, where two-thirds of those virally unsuppressed were switched to second line ART, only one-third were switched in our study.¹⁰ Adherence to national ART guidelines should be an important priority focus in routine clinical mentorship.¹¹

Four in five underwent VL test by six months and EAC in our study, consistent with findings in Harare. However, we found high proportion with VL ≥1000 copies/ml at first and repeat testing. In Swaziland, children and adolescents were more likely to have high VLs and the least likely to achieve viral suppression. This calls for ART treatment support to address adherence problems of children and adolescents.¹²

The study had some limitations. Missing last visit dates prevented computation of proportion undergoing VL test among those retained at six-months. Missing baseline characteristics precluded analysis of factors associated with not undergoing a VL test and unsuppressed VL.
In conclusion, our study points to gaps in VL monitoring among children and adolescents in Bulawayo. Future studies are needed to understand reasons for attrition along the care cascade to better target interventions.

Data availability

Underlying data

Figshare: Dataset for Moyo S et al. study: https://doi.org/10.6084/m9.figshare.c.4884726.v1

File ‘silungiledata’ contains all de-identified variables extracted for this study, alongside a codebook explaining all fields and field values.

Acknowledgements

We acknowledge Anna Fambira for her support in data extraction.

Disclaimer

The views represented here are those of the authors and do not represent the institutions they are affiliated to.

References


I think that this manuscript is addressing a very important gap in knowledge that is relevant for the current ‘treat all’ recommendations. They accessed the gaps in routine viral load monitoring at six months for children and adolescents who initiated antiretroviral therapy in a hospital in Zimbabwe. Their sample number is good enough for this analysis. The manuscript is very well written, it is very clear and concise. The study was based on analysis of secondary data which was approved by IRB.

I only have one comment that need clarification- the authors keep comparing their analysis with a study done in Harare and it is not clear whether this study that they are comparing to was conducted on adult population or the same population as they describe in their analysis. This needs to be clarified. In addition, they need to explain what could be accounting for the differences found.

Is the work clearly and accurately presented and does it cite the current literature? Yes

Is the study design appropriate and is the work technically sound? Yes

Are sufficient details of methods and analysis provided to allow replication by others? Yes

If applicable, is the statistical analysis and its interpretation appropriate? Yes

Are all the source data underlying the results available to ensure full reproducibility?
No source data required

**Are the conclusions drawn adequately supported by the results?**
Yes

**Competing Interests:** No competing interests were disclosed.

**Reviewer Expertise:** Immunology, HIV,

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Reviewer Report 28 April 2020

https://doi.org/10.5256/f1000research.25113.r61601

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Brian van Wyk
School of Public Health, University of the Western Cape, Cape Town, South Africa

The study reports on viral load monitoring at 6 months for of children and adolescents who were initiated on HIV treatment in a tertiary hospital in Bulawayo. The study is important because of the HIV epidemic in Zimbabwe, and the need to reach the third 90 of UNAIDS 90-90-90 targets.

The methodology is sound and clearly reported on. Appropriate statistical analysis is done, and these are aligned with the objectives of the study.

Few other sociodemographic and clinical factors were collected and analysed; which is a limitation to the study. This should be indicated.

In the discussion, enhanced adherence counseling is mentioned as being implemented in the hospital. However, little information on this is provided in the background. Also, it would be useful if the analysis could report on how many of the current cohort received enhanced adherence counseling.

**Is the work clearly and accurately presented and does it cite the current literature?**
Yes

**Is the study design appropriate and is the work technically sound?**
Yes

**Are sufficient details of methods and analysis provided to allow replication by others?**
Yes

**If applicable, is the statistical analysis and its interpretation appropriate?**
Yes

**Are all the source data underlying the results available to ensure full reproducibility?**
Yes

**Are the conclusions drawn adequately supported by the results?**
Yes

**Competing Interests:** No competing interests were disclosed.

**Reviewer Expertise:** HIV/AIDS; Health Systems; Adolescent Health

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

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**Author Response 29 Apr 2020**

**Hemant Deepak Shewade,** International Union Against Tuberculosis and Lung Disease (The Union), Paris, France

Thank you very much for your constructive comments.

Reviewer
Few other sociodemographic and clinical factors were collected and analysed; which is a limitation to the study.

Authors
We have included this and mentioned it as a limitation in the last but one paragraph of the discussion section. We hope this is fine.

Reviewer
In the discussion, enhanced adherence counseling is mentioned as being implemented in the hospital. However, little information on this is provided in the background. Also, it would be useful if the analysis could report on how many of the current cohort received enhanced adherence counseling.

Authors
We have information regarding when enhanced adherence counseling is provided in the settings section. We hope this is fine. We have provided information regarding how many received enhanced adherence counselling in this cohort. Please see figure 1.

We hope our response is satisfactory and the current version does not require any edits. Hence, we are not submitting a revised manuscript.

**Competing Interests:** None
Obinna Ikechukwu Ekwunife
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This short report aimed to assess the gaps in routine VL monitoring at six months for children (0-9 years) and adolescents (10-19 years) newly initiated on anti-retroviral therapy from Jan 2017 to Sep 2018.

This study is essential as such data is needed to assess how programs are fairing with regards to the UNAIDS 90-90-90 target.

The study was succinctly reported. All the essentials results based on their study objective were addressed. The study should be accepted.

Is the work clearly and accurately presented and does it cite the current literature?
Yes

Is the study design appropriate and is the work technically sound?
Yes

Are sufficient details of methods and analysis provided to allow replication by others?
Yes

If applicable, is the statistical analysis and its interpretation appropriate?
Yes

Are all the source data underlying the results available to ensure full reproducibility?
Yes

Are the conclusions drawn adequately supported by the results?
Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Pharmacoeconomics, evidence-based public health

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.
Author Response 29 Apr 2020

Hemant Deepak Shewade, International Union Against Tuberculosis and Lung Disease (The Union), Paris, France

Thank you for the constructive comments

Competing Interests: None

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