Prevalence and Consequences of Low-level Viremia Among Adolescents Living with HIV in South Africa: A longitudinal cohort study

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BACKGROUND

- Low-level viremia (LLV), defined by the World Health Organization as viral load between **51-999 copies/mL**, has been shown to be associated with an increased risk of virological non-suppression (VNS) and failure among adults on antiretroviral therapy (ART).
- Adolescents living with HIV (ALHIV) on ART are more likely to have poor adherence and HIV treatment outcomes compared to adults.
- There is limited data on the risk of progression to virological failure among ALHIV.
- We aimed to assess the prevalence of low-level viremia among ALHIV on ART and their risk of progression to virological failure.

METHODS

- We analysed viral load data from a longitudinal cohort study of ALHIV (aged 10-19 years at baseline in 2014/2015) captured by the National Health Laboratory Services (NHLS) in South Africa.
- We calculated the prevalence of LLV at the first viral load test for all adolescents with results.
- Guided classification:
    1. Undetected VL - **≤50 copies/mL**
    2. LLV - **51-999 copies/mL**
    3. Non-suppressed VL - **≥1000 copies/mL**
- We then tested which socio-demographic factors were associated with LLV at first test in those with at least 1 viral load result using a mixed-effects logistic regression.
- Among ALHIV who had at least 3 consecutive viral load tests, we assessed the relationship between LLV (at first test) and **virological failure (defined as two consecutive viral loads ≥1000 copies/mL)** using cox proportional hazards regression.

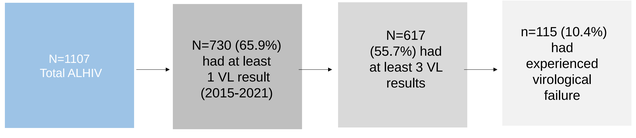


Diagram 1. Viremia analysis sample flow and inclusion criteria. VL = viral load.

The prevalence of LLV increased from 10.4% in 2015 to 13.6% in 2021 at first test among ALHIV on ART.

Adolescents experiencing LLV were 3 times more likely to progress to virological failure compared to those with those who had undetected viral loads.

RESULTS

- Prevalence of LLV increased from 10.4% in 2015 to 13.6% in 2021 at first test (baseline).
- Adolescents aged 15-20 (aOR:1.63; CI:1.20-2.22) were more likely to have low-level viremia compared to those under 15 years of age. Those aged 20 years and older also had higher odds of LLV (aOR:1.38; CI:0.88-2.16) compared to those under 15 years of age, although not statistically significant.
- Among ALHIV who had at least three consecutive viral load records, 13.3% had LLV at the first viral load and 17.1% of those with LLV had progressed to virological failure.
- Poor adherence (aHR:0.86; CI:0.84-1.99), adolescents aged 15-20 (aHR:1.53; CI:1.00-2.34), LLV (aHR: 3.35; CI:1.58-7.10) and VNS (aHR:16.33; CI:9.34-28.56) were strongly associated with virological failure.
- Kaplan-Meier survival analysis demonstrates that LLV patients have a better survival trajectory compared to those virologically non-suppressed but worse than those with undetected results.

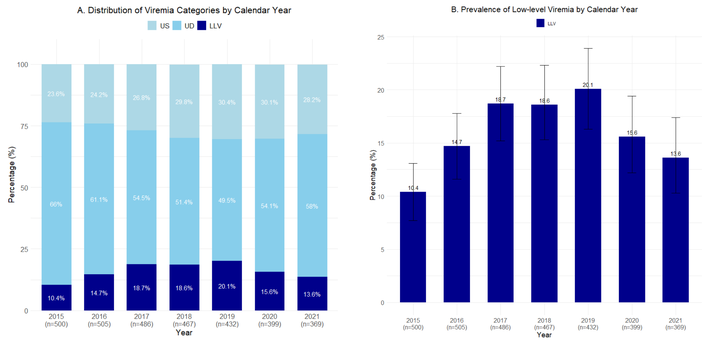


Figure 1. Distribution of Viremia by Calendar Year. VNS = virological non-suppression, UD= undetected viral load and LLV = low-level viremia. *Prevalence was calculated using the first viral load test result for each participant within a given year.

Figure 2. Adjusted Hazard Ratios for Virological Failure. ART = antiretroviral therapy. *All variables found to be statistically significant are marked with an asterisk. Reference groups: (1) Undetectable viral load; (2) Non-adherence; (3) Age <15; (4) Male; (5) Horizontal HIV infection; (6) Urban; (7) Non-biological parent; (8) ART <12m. ART duration was measured in months. Adherence was self-reported and included as the closest recorded adherence record available in relation to the test date. All the abovementioned variables including the viral load test year were adjusted for in the analysis.

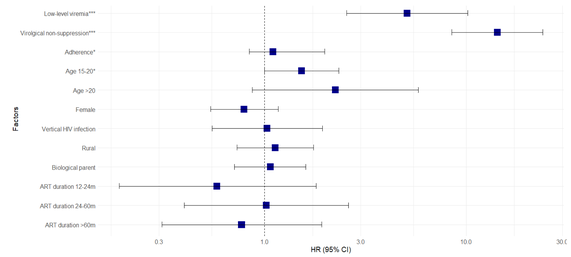
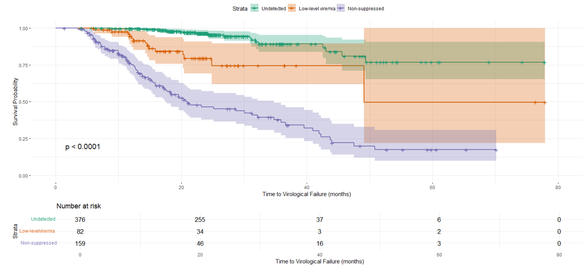


Figure 3. Kaplan Meier Survival Graph for Progression to Virological Failure by Viremia Category. Survival analysis demonstrates significant differences (p<0.0001) in the time to virological failure across the three viremia categories. Time was measured in months and was calculated as the difference between third and first viral load test date.



CONCLUSIONS

- The prevalence of LLV among ALHIV on ART is high
- LLV strongly predicts virological failure.
- Older adolescents (aged 15-20) have higher odds experiencing LLV compared to younger adolescents.
- Enhanced adherence support among ALHIV with LLV - not just those with viral non-suppression – is needed to prevent virological failure.

LIMITATIONS

- Routine viral load data may introduce variability in testing intervals and result accuracy.
- Confounding factors like drug regimen and co-morbidities may influence observed associations

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