

Persistent Low-level Viremia is Associated with Increased Risk of Virologic Failure and Mortality



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ABSTRACT: Detection of transient or persisting low-level viremia with plasma viral load >50 c/mL remains common amongst patients receiving ART. The purpose of this study was to evaluate the effect of ongoing viremia on risk of virologic rebound and mortality. **Methods:** Data were derived from a multi-site Canadian cohort of HIV+ patients >18 years receiving ART between 01/2000 and 12/2008. Patients who achieved 2 consecutive pVL <400c/mL at least 30d apart, with >6 subsequent pVL over 24 months of classification period (CP) were placed into 4 groups. Group 1 (fully suppressed) maintained pVL <50c/mL throughout CP. Group 2 (transient viremia) achieved pVL <50c/mL, and remained <50c/mL for >75% of CP, with 25% viremic (50-1000c/mL). Group 3 (short-term viremia) maintained <50c/mL for 25-75% of CP with the remainder viremic. Group 4 (long-term viremia) maintained pVL <50c/mL for <25% of CP with the remainder viremic. After the initial CP, patients were followed to determine time to viral rebound and time to death using Cox proportional hazards models. **Results:** Of 1674 patients, 84% were male, and median age was 41. Compared to Group 1, those in Group 2 had similar risk of subsequent viral rebound (HR 1.12; 95%CI 0.62-2.01), while Group 3 (HR 6.05; 95%CI 4.06-9.02) and Group 4 (HR 20.46; 95%CI 11.4-36.74) were more likely to experience virologic rebound. Those experiencing short-term low-level viremia (subset with majority pVL <200c/mL within Group 3) were more likely to have associated viral rebound (HR 4.95; 95%CI 2.29-10.69) and mortality (HR 4.25; 95%CI 1.41-12.82) compared to those with the same pVL range but experiencing only transient viremia (within Group 2). **Conclusion:** Those experiencing short-term viremia were more likely to have subsequent viral rebound. Those experiencing short-term low-level viremia were more likely to have subsequent rebound and death compared to those experiencing transient low-level viremia.

Introduction

- Detection of transient or persisting viremia remains common amongst patients receiving antiretroviral therapy (ART), with reported rates of transient viremia in 27-40% of patients, and persisting viremia in 12%^{1,2}.
- The impact of persisting low-level viremia (pVL 50-400copies/mL) is less clear.
- The purpose of this study was to evaluate the effect of differing levels and durations of ongoing viremia on the risk of subsequent virologic rebound and mortality.

Methods

- Adult patients > 18 yrs receiving ART between Jan 1, 2000 and Dec 31, 2008 in a multi-site Canadian cohort were included.
- Patients who achieved 2 consecutive pVL <400c/mL at least 30d apart with ≥ 6 subsequent pVL over a 24 month classification period (CP) were placed into 4 groups based on virologic response to ART:
 - **Group 1 (Full Suppression):** maintained pVL<50c/mL throughout CP.
 - **Group 2 (Transient Viremia):** achieved pVL<50c/mL and remained with pVL <50c/mL for ≥ 75% of CP, with 25% viremic 50-1000c/mL.
 - Subset (Transient low-level Viremia): those with majority pVL <200c/mL when viremic.
 - **Group 3 (Short-term Persisting Viremia):** maintained pVL<50c/mL 25-75% of CP, with the remainder viremic.
 - Subset (Persisting low-level Viremia): those with majority pVL <200c/mL when viremic.
 - **Group 4 (Long-term Persisting Viremia):** maintained pVL<50c/mL for ≤25% of CP, with the remainder viremic.
- After the initial CP, patients were followed to determine time to viral rebound (2 consecutive pVL>1000c/mL) and time to death using adjusted Cox proportional hazard models.

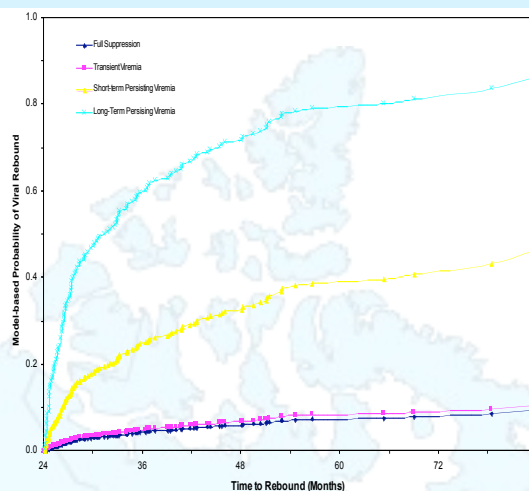


Figure 1. Probability of viral rebound among those with transient and persisting viremia.

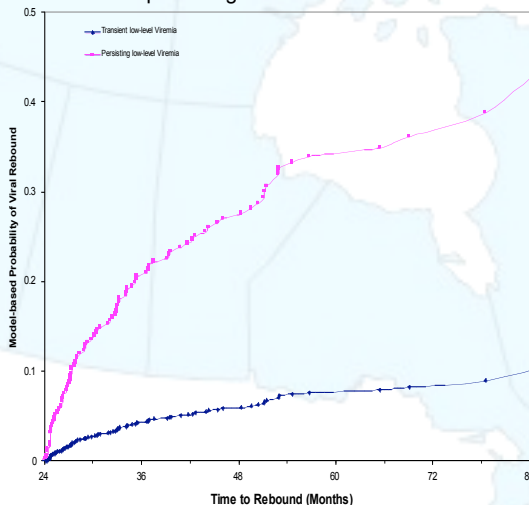


Figure 2. Probability of viral rebound among those with transient or persisting low-level viremia

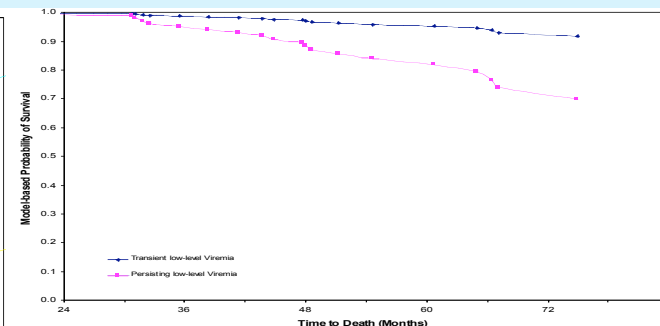


Figure 3. Probability of survival associated with persisting low-level viremia

Results

- 1674 patients met criteria for inclusion.
- 84% were male, and median age was 41 (interquartile range [IQR] 35-47).
- From time of initial suppression, median follow-up time for virologic rebound (n=1674) was 36 months (IQR 25-53). Median follow-up time for mortality outcomes (n=1430) was 51 months (IQR 35-70).
- Compared to Group 1(Full Suppression), those in Group 2 (Transient Viremia) had similar risk of subsequent viral rebound (hazard ratio [HR] 1.12; 95% CI 0.62-2.01).
- Compared to Group 1, those in Group 3 (Short-term Viremia) (HR 6.05; 95CI 4.06-9.02) and Group 4 (Long-term Viremia) (HR 20.46; 95% CI 11.40-36.74) were more likely to experience viral rebound (Figure 1).
- Those experiencing short-term low-level viremia (Group 3 subset) were more likely to have associated viral rebound (HR 4.95; 95% CI 2.29-10.69) and mortality (HR 4.25; 95% CI 1.41-12.82) compared to those with transient low-level viremia (Group 2 subset) (Figure 2,3).

Conclusions

- Sustained virologic suppression remains an important target for ART therapy.
- Those patients experiencing persisting viremia (short-term and long-term) were more likely to experience subsequent viral rebound.
- Patients with only short-term low-level viremia remained at higher risk of virologic rebound and increased mortality compared to those with full suppression or only transient low-level viremia.

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