**Monitored Viral Load: A Measure of HIV Treatment Outcomes in an Outpatient Setting in Rhode Island**

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**ABSTRACT**

Community viral load measurements have been postulated to be a population-based biomarker of HIV disease. We propose the use of the monitored community viral load (mCVL) as an aggregate measure of viral load among persons receiving HIV care with available HIV-1 plasma viral loads and applied it to our clinic population from 2003-2010. We demonstrated a reduction in mCVL from 16,589 copies/ml to 11,992 copies/ml that correlated with a rising rate of antiretroviral use and HIV viral suppression; however, differences among risk populations were observed. The mCVL is a useful measure of HIV burden among patients in care; it may reflect the HIV transmission risk in the community and help target preventive interventions.

**KEYWORDS:** Community viral load, HIV, Rhode Island, Antiretroviral therapy

**INTRODUCTION**

Antiretroviral therapy (ART) effectively suppresses HIV-1 RNA concentrations in blood and other body fluids, hence decreasing the risk of HIV infectivity.1,2 Based on this principle, universal HIV testing and early antiretroviral therapy has been advocated as a strategy to lower HIV incidence. Clinical evidence and mathematical models support the use of ART to control HIV transmission risk at an individual and population level.3,4

The concept of community viral load (CVL), defined as the mean or total HIV-1 plasma viral load (PVL) of infected individuals in a given geographic area or population, has been postulated as a useful population-based measure of the effect of treatment on HIV transmission and supported by ecological evidence.5,6,8 As a result, the Division of HIV/AIDS Prevention at the Centers for Disease Control and Prevention (CDC) has proposed the use of CVL as a tool to monitor the progress of the National HIV/AIDS Strategy goals and released guidelines to standardize definitions and calculations in 2011.9,10 Nonetheless, CVL measurements must include PVLs from all HIV-infected persons, including those who are not engaged in care, in order to accurately assess the population’s aggregate viremia. We propose the use of the “monitored community viral load” (mCVL) instead, an estimate that includes patients in care with available PVLs, to examine HIV transmission drivers and quality of HIV care in a community-based outpatient practice.10

**METHODS**

This is a retrospective analysis of clinical and demographic data collected from a longitudinal electronic database of all HIV-infected individuals receiving care at the Miriam Hospital Immunology Center, the largest HIV care provider in RI, with approximately 1,500 active patients in 2012.11,12 We determined the proportion of patients on ART with undetectable HIV-1 plasma viral load (PVL), with CD4 cell counts below 200 and ≥ 350 cells/μL (based on the last available CD4 cell count each year), and the proportion retained in care between January 1, 2003 and December 31, 2010. ART use was defined as documentation of prescribed ART in at least one clinic visit in any given year. Given variability in the level of detection among viral load assays used over time, an undetectable PVL was defined as < 75 copies/ml. Patients who attended at least 1 clinic visit with a medical provider within each 6-month period in a given year separated by ≥ 60 days were considered retained in care.

Based on the CDC guidance, mean and median mCVLs were calculated using detectable and undetectable PVL values among patients in-care.10 To be included in this analysis, patients must have had at least one PVL value recorded in a given year during the study period. Calculations were compared using three different PVL summary measures: 1) the mean of all available individual PVLs for each calendar year; 2) the aggregate mean of the annual mean PVL for each individual; and 3) the mean of the last available PVL for each individual per calendar year. The latter was used to assess changes in mCVL among patients stratified by HIV risk factor and to assess trends over time.

We summarized the demographics and clinical characteristics such as gender, age, race/ethnicity, HIV risk factor, proportion on ART, CD4 counts ≥ 350 cells/μL, retention in-care rates, and mCVL for the total sample from 2003 to 2010 using means (standard deviation) for continuous data and absolute numbers (percentages) for categorical variables. Ordinary Least Square linear regression models were used to assess time trends treating years as an independent variable. A regression coefficient estimated the changes over time; each series was analyzed independently. All data analysis was
conducted using Statistical Analysis Software (SAS) version 9.1 (Cary, NC), double sided p-values and a threshold for statistical significance set at < 0.05.

RESULTS

A total of 1959 unique HIV-infected patients received care at our center during the study period. As shown in Table 1, the number of active patients in-care increased from 922 in 2003 to 1,383 in 2010, particularly men who have sex with men (MSM) as reflected by the regression coefficient (p < 0.01).

Over the time period, the clinic population was predominantly Caucasian, non-Hispanic males, between 25-64 years of age. MSM and heterosexual contact were the most common HIV risk factors recorded. Eighty-five to 95% of patients had at least one PVL in a given year from 2003 to 2010.

The proportion of patients receiving ART increased from 67% to 86% by the end of the study [p < 0.01]. This finding correlates with a 22% increase in the proportion of patients with undetectable viral loads [p < 0.01] and a 12% rise in the proportion with CD4 counts ≥ 350 cells/μL [p < 0.01] over the 8-year period (Figure 1). The clinic population retention in-care rate remained stable, ranging from 61% to 68%, with similar trends observed across risk groups (Table 1).

We calculated the mCVL using the three calculation methods described and found there was a decrease in mCVL...
over time using each calculation method (Table 2). Using the aggregate mean of the last available PVL for each calendar year per individual, we observed decline in the mCVL from 16,589 copies/ml in 2003 to 11,992 copies/ml in 2010 [p = 0.07] as shown in Table 3. When looking at the mCVL among risk groups over the time period, there was a significant reduction in mCVL over the time period among MSM [p = 0.035] but not among other risk groups [p = 0.14].

Figure 1. Percentage of clinic patients on ART, with undetectable PVL and CD4 cell count ≥ 350 cells/μL over study period (2003-2010).

Table 2. Comparison of Monitored Community Viral Load Calculation Methods.

<table>
<thead>
<tr>
<th>mCVL Calculation Methods</th>
<th>2003</th>
<th>2004</th>
<th>2005</th>
<th>2006</th>
<th>2007</th>
<th>2008</th>
<th>2009</th>
<th>2010</th>
<th>Mean (SD)*</th>
<th>R Coefficient (SD, P Value)**</th>
</tr>
</thead>
<tbody>
<tr>
<td>Method #1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>-1578 (283.6, &lt;0.01)</td>
</tr>
<tr>
<td>Method #2</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>-1191 (404.6, 0.03)</td>
</tr>
<tr>
<td>Method #3</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>-977 (441.1, 0.07)</td>
</tr>
</tbody>
</table>

1 Mean of all available individual PVLs for each calendar year.
2 Aggregate mean of the annual mean PVL for each individual.
3 Mean of the last available PVL for each calendar year per individual.
* Across years.
** Regression coefficient, P value by ordinary linear regression.

Table 3. Monitored Viral Load Over Time by HIV Risk Factor.

<table>
<thead>
<tr>
<th>Year</th>
<th>2003</th>
<th>2004</th>
<th>2005</th>
<th>2006</th>
<th>2007</th>
<th>2008</th>
<th>2009</th>
<th>2010</th>
<th>RCoefficient* (SD, P value)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean mCVL</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>- 977.0 (441.1, 0.07)</td>
</tr>
<tr>
<td>MSM (SD)</td>
<td>16,139 (51,766)</td>
<td>20,946 (61,058)</td>
<td>20,197 (63,342)</td>
<td>20,052 (70,941)</td>
<td>19,151 (73,021)</td>
<td>13,733 (53,485)</td>
<td>11,565 (40,001)</td>
<td>11,176 (67,742)</td>
<td>-1217 (450.6, 0.035)</td>
</tr>
<tr>
<td>Non-MSM (SD)</td>
<td>16,770 (55,658)</td>
<td>20,323 (60,806)</td>
<td>14,867 (54,846)</td>
<td>16,150 (59,687)</td>
<td>21,888 (182,023)</td>
<td>14,407 (59,016)</td>
<td>11,074 (51,844)</td>
<td>12,507 (94,389)</td>
<td>- 848.9 (503.6, 0.14)</td>
</tr>
</tbody>
</table>

1 Using the last available PVL for each calendar year per individual.
2 MSM – Non-MSM.
* Regression Coefficient, P value by ordinary linear regression.

Abbreviations: mCVL, Monitored community viral load; SD, standard deviation.
DISCUSSION

The demographics and risk factor characteristics of our HIV population is comparable to the surveillance profile of RI’s HIV/AIDS epidemic; the majority of cases occurring among white MSM with a decreasing proportion of IDU.13 We detected a significant increase in ART use that correlated with improvement in HIV viral suppression rates and immune status among patients receiving care at our center between 2003 and 2010. Similar results have been reported in other large urban clinic settings nationwide.14, 15 These findings likely reflect the effectiveness of widespread and earlier implementation of ART in response to national treatment guidelines.16

The increased proportion of patients on ART and those who achieved a suppressed HIV-1 viral load resulted in a concurrent downtrend of the mCVL over time. The decline of mCVL provides additional insight into the quality of our HIV care and implies a decrease in the HIV transmission potential of the clinic population and possibly at a broader community level.17, 18 Several studies have shown an association between a decrease in the CVL and a reduction in new HIV infections in populations such as San Francisco and British Columbia.6,8 Although our results are derived from a single center and are not necessarily generalizable to the entire state, there was a concurrent decline in the number of new HIV diagnoses reported to the RI Department of Health during this time period (178 new diagnoses in 2004 to 106 new diagnoses in 2010) raising the possibility that improved HIV viral control among our clinic population correlates with a reduction in new HIV diagnoses statewide.13

CVL has been used as a public health monitoring tool of the HIV epidemic.5–9 We believe the mCVL is particularly useful as a research and surveillance tool of community-level interventions that can be easily implemented in HIV care centers. It is methodologically feasible, reproducible, and is less affected by incomplete data. Nonetheless, we recognize that interpretation of the mCVL has several limitations as it excludes persons with undiagnosed HIV, those who are not engaged in care, and those who are engaged in care but do not have available PVL test results. As an ecological measure, population level observations can be mistakenly interpreted to reflect outcomes of individuals in that population.18, 19 In addition, CVL calculations usually use one viral load value from each patient collected during a given calendar year but most patients in care will have several viral load measures and the selection of a single value could affect the accuracy of the result. For this reason, we compared three different mCVL calculation methods including multiple viral load values available for each patient per year and found a uniform decline of the mean mCVL over time using all three methods. It is evident that using the mean of the last available PVL for each calendar year per individual resulted in the lowest mCVL mean and standard deviation value and appears to be comparable to calculations used in other studies.7, 8, 17

While the downward trend of our mCVL reflects the remarkable impact of increased ART implementation and uptake in this urban HIV-infected population, there is a concern for persistent high disease burden among certain risk populations such as IDU, heterosexuals, and among persons classified as having “other” risk factors. HIV treatment as a prevention strategy can only be successful if all of the sequential steps of the HIV treatment cascade (HIV diagnosis, linkage to care, retention in care, ART receipt, and viral suppression) are optimized.20, 21 Further research is needed to explore HIV treatment and retention in care among non-MSM persons in RI, given we did not observe a significant decline in mCVL over time among these risk groups. Despite MSM being the predominant risk factor among newly diagnosed HIV cases in RI, we observed a downturn of the mCVL among MSM receiving care at our center.13 A possible explanation for this discrepancy is that there could be a substantial population of undiagnosed HIV positive MSM in the community, or MSM who are aware of their HIV infection yet who are not engaged in care, who are contributing to ongoing HIV transmission in RI.

In summary, increased use of ART and the subsequent HIV viral suppression correlated with a decrease in the mCVL in our patient population. The mCVL is a useful indicator of clinical HIV care within a population engaged in treatment and may be helpful in estimating the infectiousness of a population receiving HIV care.

References


Meeting Data Presented

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