Impact of Testing Delay on Low-level Viraemia in South Africa: A Programme-wide View

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Background

- Low-level viraemia (LLV) can be common in HIV-infected individuals receiving antiretroviral therapy (ART) and has been shown to be associated with increased risk of virologic failure following sustained virologic suppression.
- Analytic performance of high throughput commercial viral load (VL) assays starts to deteriorate when there is delay in plasma separation (>6 hours) and delay in VL testing (>24 hours)
- In large ART programmes where VL testing is centralised, delay in sample processing could affect the detection of these LLV due to sample degradation.

Methods

- We examined the frequency of LLV in patients on ART in the public health care system of the Western Cape province, South Africa from 2009-2015 using routine laboratory VL data from the National Health Laboratory Service at Groote Schuur and Tygerberg laboratories.
- Abbott RealTime HIV-1 assay (Abbott Laboratories, Des Plaines, IL USA) was used during this study period.
- We analysed the proportion of various categories of VL test results by time to sample processing (<48 hours to 10 days in 24h increments) over this period. The sample processing time is measured by turnaround time (TAT) between the estimated time of collection and the time of test completion.
- The VL categories analysed were:
  - LLV: defined as any detectable VL <400 copies/mL.
  - VL result between 400-1000 copies/mL.
  - Virologic failure defined as VL >1000 copies/ml
- In order to analyse confounding effects, results were further stratified by calendar year, testing day of the week and healthcare facility size.
- Size of facility is determined by the total number of test performed (small <1000 tests; medium 1000-9999 tests and large >10,000 tests)

Results

- We analysed 1,067,153 VL episodes from 509 facilities.
- We identified 208,694 samples with LLV (19,6%), 27,431 samples (2.6%) had detectable viral load between 400-1000 cp/ml and 183,413 (17.2%) VL result were >1000 cp/ml.

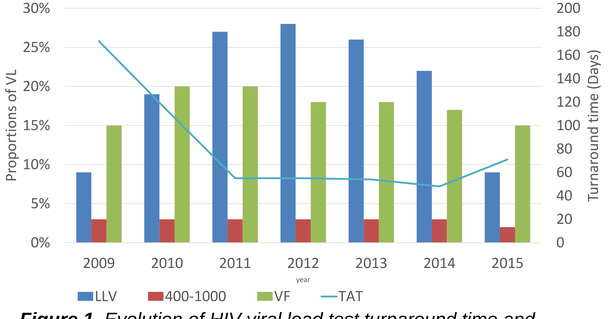

Figure 1. *Evolution of HIV viral load test turnaround time and proportion of low level viraemia (LLV) and virologic failure in the western cape. The median TAT had significantly reduced from 173 hours in 2009 to 71 hours in 2015, the proportion of virologic failure remained relative constant over the study period but the low level viraemia fluctuated significantly during this period.*

	Monday	Tuesday	Wednesday	Thursday	Friday
All facilities					
N=	191571	235489	234300	236702	164824
% VS	60.4%	61.2%	60.2%	60.4%	59.8%
% LLV	19.7%	19.5%	19.3%	19.7%	20.1%
Median TAT	55.2hrs	56.2hrs	62hrs	76.8hrs	92.3hrs
Large facilities					
N=	75351	92706	90020	93422	65745
% VS	63.1%	64.1%	63.4%	63.4%	61.7%
% LLV	18.6%	18.3%	17.7%	18.5%	18.9%
Median TAT	53.7hrs	55hrs	55.9hrs	95.5hrs	93.2hrs
Medium Facilities					
N=	97871	121423	119933	121434	83425
% VS	59.7%	60.7%	59.8%	59.4%	59.6%
% LLV	20.5%	20.3%	20.5%	20.6%	20.9%
Median TAT	55.6hrs	57.9hrs	63.2hrs	95.5hrs	93.2hrs

Table 1 *Viral load testing by days of the week. Compared to the Monday-Wednesday samples, viral load taken on Thursday and Friday has substantially longer turnaround time(TAT). However, the proportion of low-level viraemia (LLV) and virologically suppressed (VS - VL<20 copies/ml) individuals remained similar.*

- Samples with increased TAT are associated with less frequent detection of LLV. The decrease in detection is observed in sample with TAT>48 hours. While 23.8% of samples tested within first 48 hours had LLV, the proportions of LLV were 21.4%, 20.1%, 19.6% and 17.8% for samples tested on day 3, 4, 5 and 6 respectively.

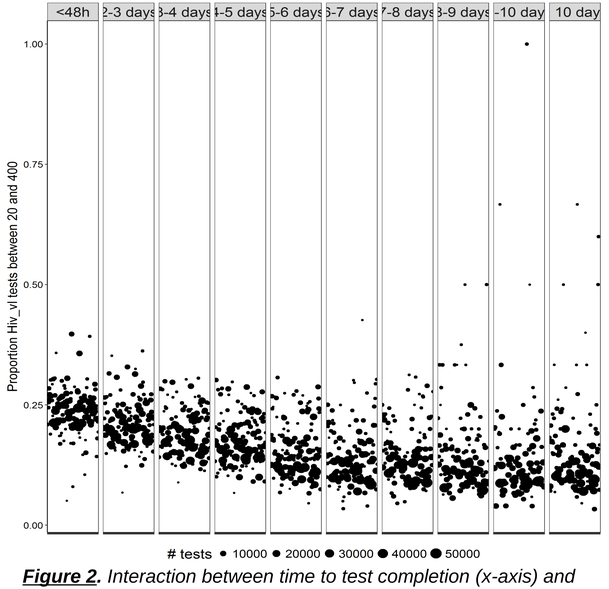

Figure 2. *Interaction between time to test completion (x-axis) and proportion of samples with low-level viraemia (y-axis) in medium and large health facilities in Western Cape, South Africa. Each dot represent a facility. The size of the dot represent the size of the facility according to numbers of tests per annum.*

- Further delays in testing did not result in significant changes in the frequency of LLV. The decrease in LLV detection rate over time remained despite taking size of facility and calendar years into consideration. These trends were not observed for VL results between 400-1000 copies/mL, with 3% detected in the first 48h compared to 4% on day 6.

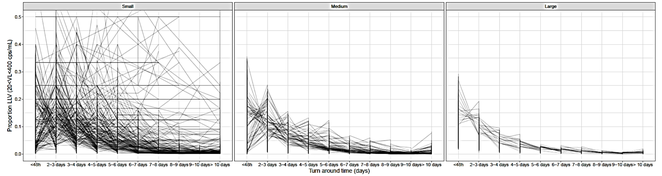

Figure 3. *Spaghetti plot of turnaround time and proportion of LLV by small, medium and large facilities. Each line represents a single facility. The trends from medium and large facilities suggest early and significant drop off in the proportion of LLV beyond the initial 48 hours.*

Discussion

- The proportion of LLV decreases as TAT increase beyond the first 48 hours, pointing to potential early programme-wide compromised sample stability prior to plasma separation and testing.
- As samples with LLV are nearer to the limit of detection of VL assays, delay in sample processing may significantly reduce the probability of correctly classifying these VLs when compared to samples in higher VL categories.
- As detection of LLV becomes more clinically relevant, the delay in testing should be minimised in VL testing programmes in order to avoid under-estimation of VL.

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