Performance of HIV viral load with dried blood spots in children on ART in Mozambique

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Background

Quantitative viral load (VL) is recommended by the World Health Organization to monitor antiretroviral treatment (ART) in HIV-infected persons and detect Virologic Failure (VF) (>1000 copies/mL); plasma VL testing is currently the gold standard. However, separation, transportation, and storage of plasma are often challenging in resource-limited settings for patients living in remote areas. Adopting less stringent sample types like finger stick dried blood spots (FS-DBS) may improve access to VL testing.

There is a limited evidence on the validity of FS-DBS to estimate VF at 1000 copies/mL and no evaluations have focused on children. Minimizing false negative misclassification is preferred clinically and programmatically to avoid delayed treatment switches and increased risk for HIV drug resistance. In this study, we compared the performance of HIV VL testing using DBS as an alternative to plasma for VL testing in children on ART in Mozambique.

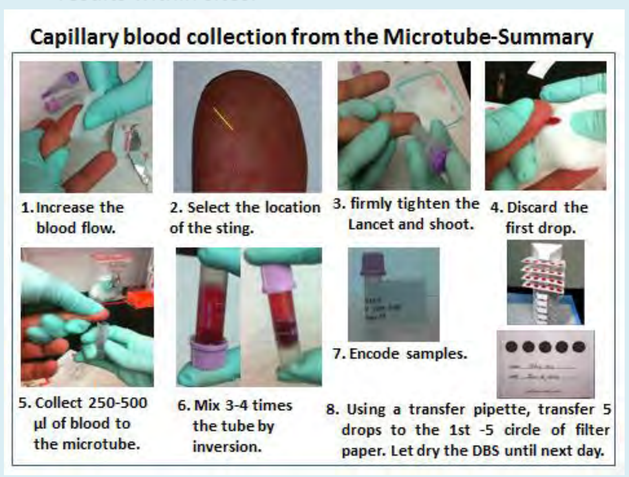
Methods

Study Design

- Cross-sectional study--children (<15 years) on ART for > 12 months in care at six high volume pediatric HIV clinics in Maputo City and Maputo Province were sequentially enrolled between August 2013 and March 2014.
- Paired plasma and FS-DBS were collected. Plasma was prepared from venous blood and for FS-DBS, blood was collected in micro-EDTA tubes by finger stick and spotted with transfer pipette using 75 µL of blood per spot.
- Plasma VL was performed using COBAS Ampliprep/COBAS TaqMan HIV-1 Test, v2.0 at National Institute of Health (INS) in Mozambique and FS-DBS VL was tested with one spot per test using Abbott m2000 HIV-1 DBS Quant, v4 in Centers for Disease Control (CDC) in Atlanta.

Analysis

- Three thresholds (≥1,000, ≥3,000 and ≥5,000 copies/mL) using DBS-FS were compared to plasma (Gold Standard) and a constant plasma threshold of ≥1,000 copies/ml.
- Sensitivity and specificity for each VL threshold were estimated.
- All statistical analysis were conducted using SAS 9.3 and STATA 13 accounting for clustering of results within sites.



Roche COBAS Ampliprep/COBAS Taqman 96



Abbot m2000 sp/ rt



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Results

The present study recruited 717 children, aged bellow 15 years old. Higher sensitivity was observed at 1000 copies/ml (79.8%) and it tended to decrease with increasing viral load threshold. Conversely, specificity was seen to increase with increasing threshold (Table 1). Lin's concordance correlation coefficient between Abbott DBS and a gold-standard (Roche) plasma assay in measuring viral load in children were 88.9 [87.4, 90.4] (p<0.05).

Table 1: Sensitivity, Specificity, Kappa, and Misclassification

Threshold (≥ copies/ml)		Sensitivity (%)	Specificity (%)	Kappa	False Positive	False Negative
Plasma: DBS	n	95% CI	95% CI	95% CI	-	-
1000:1000	717	79.8	97.6	0.79	20.2	2.4
		(61.2, 90.8)	(93.8, 99.1)	(0.72, 0.86)		
1000:3000	717	70.6	98.8	0.72	29.4	1.2
		(51.3, 84.5)	(94.2, 99.8)	(0.65, 0.79)		
1000:5000	717	63.4	99.3	0.66	36.6	0.7
		(46.9, 77.2)	(97.1, 99.8)	(0.59, 0.73)		

***False Positive**: samples that incorrectly identified VF but had a VL in plasma of less than 1,000 (upward misclassification). **False Negative:** samples that incorrectly identified virologic suppression but had a VL in plasma of over 1,000 (downward misclassification).

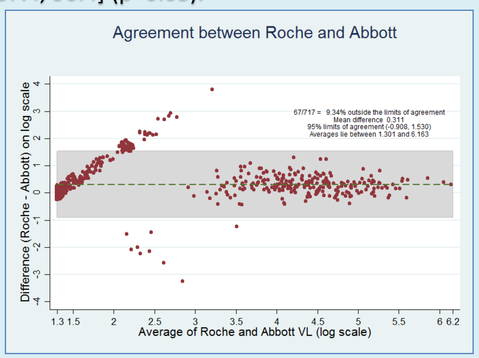

Figure 1. The correlation between Roche plasma VL and Abbott DBS for finger stick dried blood spots.

Summary and Conclusions

- Our DBS VL data demonstrated that FS-DBS specificity at 1000, 3000, and 5000 copies/ml compared to plasma was excellent, with low false positivity rates. This methodology, if used more widely, would result in few misclassifications of treatment failure.
- FS-DBS is a comparable, practical alternative to plasma for determination of VF among ART-experienced children.
- A DBS cut-off of 1,000 copies/ml is optimal, however program managers and policy makers must determine which DBS methods and VF thresholds are most appropriate based on local context and available resources with respect to supplies, management of biological waste, and human resource capacity.

Limitations

- Convenience sample of urban/peri-urban high volume facilities
- DBS evaluated for only one platform (Abbott) while multiple platforms are used nationally and regionally.

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