A point-of-care triage test for HIV virological failure: filling the gaps in viral load coverage

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Background

IFN-ɣ-induced protein 10 (IP-10) is a chemokine strongly correlated with human immunodeficiency virus (HIV) viral load (VL). A recently developed IP-10 point of care test (POCT) could serve to triage antiretroviral (ART)-treated people living with HIV (PLHIV) for virological failure (VF) thus prioritizing scarce VL testing.

Objectives

1. To evaluate the field performance of a semi-quantitative prototype lateral flow IP-10 POCT as a screening test for VF in South Africa.
2. To assess the cost-effectiveness of implementing an IP-10 POCT in a two-step algorithm to screen for VF in ART-treated PLHIV in a low-resources and low VL coverage setting using the example of Mozambique for costs.

Methods

Field performance

Participants and procedures:

- Enrollment of patients on ART for ≥1 year who attended a primary health clinic in the Western Cape.
- Collection of finger prick blood for direct application onto the IP-10 antibody-sandwich lateral flow POCT and reading the IP-10 signal with a portable Cube Reader (arbitrary units) after 20 min (index test).
- Plasma VL result at or ≤1 month prior to clinic visit (reference test).

Analysis

- IP-10 POCT values-based model constructed to identify individuals with VF (VL>1,000 copies/mL).
- Uni-and multivariable logistic regression with penalized likelihood.
- Calculation of area under the receiver operating characteristic curves (AUC) to evaluate model prediction.

Cost-effectiveness analysis

Design: A deterministic decision analysis comparing the use of VL testing only with a two-step algorithm based on IP-10 POCT screening followed by VL testing as a confirmatory test for positive results.

Study population:

- A simulated cohort of 1,000 ART-treated PLHIV 18 years of age.
- 40% of VL coverage and 24% of VF prevalence.

Effectiveness outcomes and costs:

- Health effects: Disability Adjusted Life Years (DALYs) and new HIV infections averted.
- Costs to the health care provider associated with HIV, including test costs (US$ 3 for the IP-10 POCT and US$ 51 for the VL test), were based on Mozambique.

Time horizon: 1 year, no discount rate.

Results

Figure 1a. Performance of IP-10 POCT values models in predicting VF.

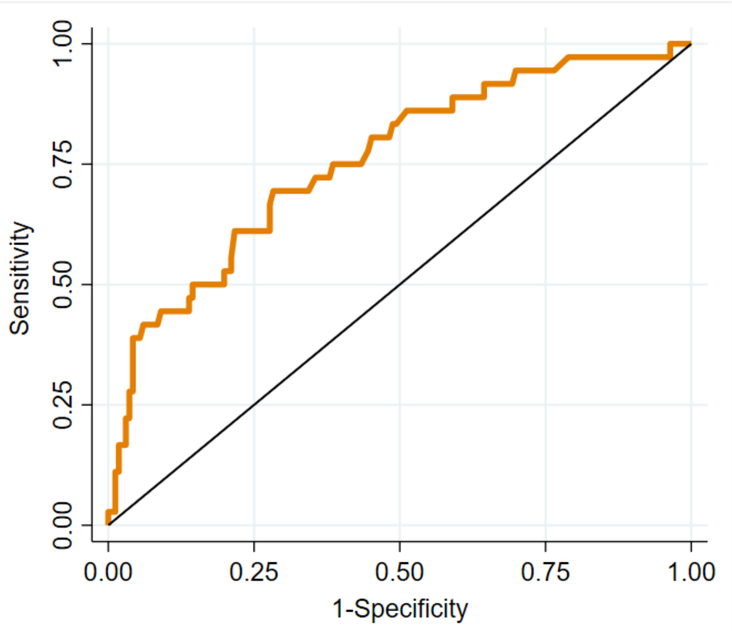

Figure 1b. Cut-off IP-10 POCT values with their respective sensitivity and specificity values.

Cut-off value	Sensitivity (%)	Specificity (%)
7.3	100.0	3.5
10.9	97.3	20.5
12.0	94.6	29.2
12.8	91.9	35.1
13.6	88.2	40.9
14.6	86.5	49.1
14.9	83.8	51.5
16.1	81.1	55.0

- Among the 209 participants (median age 38 years and 88% female), 18% had VF. Median IP-10 POCT values were higher among individuals with VF compared to those without (24.0 vs. 14.6; p<0.001).
- Among those individuals (n=57) with detectable VL (>50 copies/mL), IP-10 values showed a significant moderate correlation with VL (ρ=0.46, p<0.001). The IP-10 POCT predicted VF with an AUC=0.76 (95% confidence interval (CI), 0.67–0.85) (figure 1a).
- Using a cut-off value of ≥12.8 (a sensitivity above 90% was prioritized), the model identified VF with 91.9% sensitivity (95% CI, 78.1%-98.3%) and 35.1% specificity (95% CI, 28.0%-42.7%) (figure 1b) resulting in a positive predictive value of 23.4% (95%CI, 16.8-31.2) and a negative predictive value of 95.2% (95%CI, 86.7-99.0) in a setting with 18% prevalence of VF.
- IP-10 POCT values, ART adherence and time since HIV diagnosis were the only factors associated with VF (table 1).
- The implementation of an IP-10 POCT triage test for VF could avert more than 30% of the DALYs associated with HIV, 8.5 out of 10 new HIV infections and savings from US$ 46,339 to US$86,701 to the health system per 1,000 PLHIV tested. The settings which would benefit the most are those with low VL coverage and high VF prevalence.

Table 1. Sociodemographic and clinical characteristics associated with VF.

	n (%) or median (IQR)						Odds Ratio	95%CI
	Total (n = 209)		VL≤1000 copies/ml (n = 171)		VL>1000 copies/ml (n = 37)			
IP-10 POCT values (n=208)	16.2	(11.9-22.8)	14.6	(11.3-20.0)	24	(17.6-36.3)	2.38*	1.66-3.40
Years since HIV diagnosis	7	(4-10)	6	(4-9)	8	(5-12)	1.11	1.01-1.22
Missed ART								
None	182	(87.08)	158	(91.86)	24	(64.86)	Ref.	
At least once a month	27	(12.92)	14	(8.14)	13	(35.14)	6.02	2.56-14.16

**Change by 10 units*
IQR: Interquartile range

Conclusions

The IP-10 POCT is an effective and cost-effective triage test for routine VL monitoring. Combining a highly sensitive, low-cost IP-10 POCT-based screening with VL testing in a two-step decision algorithm could provide a greatly needed monitoring tool in settings with low VL coverage, and result in significant improvement in ART monitoring and savings for health systems.

Presented at AIDS 2022 – The 24th International AIDS Conference

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