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Short Communication: Low False Recent Rate of Limiting Antigen-Avidity Assay Combined with HIV-1 RNA Data in Botswana

Sikhulile Moyo,[1,2] Kenanao P. Kotokwe,[2] Terence Mohammed,[2] Corretah Boleo,[2] Lucy Mupfumi,[2] Samuel Chishala,[1,3] Lesedi Tsalaile,[1] Hermann Bussmann,[2,4] Simani Gaseitsiwe,[2,4] Rosemary Musonda,[2,4] Joseph Makhema,[2,4] Marianna Baum,[5] Richard Marlink,[2,4] Susan Engelbrecht,[1,6] Max Essex,[2,4] and Vladimir Novitsky[2,4]

Abstract

Cross-sectional estimation of HIV incidence could misclassify some established or chronic HIV infections as recent. Usually long-term nonprogressors, elite and viremic controllers, and individuals on ART contribute to misclassification. Local data on the false recent rate (FRR) could minimize misclassification during estimation of HIV incidence. To improve monitoring of HIV incidence, we estimated local FRR in Botswana. A total of 1,036 specimens from individuals infected for at least 1.5–2 years were sampled between 2004 and 2009 and tested using the limiting antigen (LAg)-avidity assay using a cutoff of 1.5 normalized optical density units. The FRR was 0.97% (10/1,036; 95% confidence interval [CI] 0.46–1.77). Four samples had HIV-1 RNA >1,000 cps/ml, giving an adjusted FRR of 0.39% (4/1,036; 95% CI 0.11–0.99). A combination of LAg and HIV-1 RNA load data resulted in FRR below 1% in the Botswana population.

Keywords: false recency rate, limiting antigen assay, HIV incidence, HIV recency, cross-sectional incidence

HIV INCIDENCE ESTIMATES ARE critical for monitoring HIV transmission trends and evaluating the impact of interventions.[1] Assays for cross-sectional surveillance of HIV incidence are greatly needed because of the high costs and extended time needed to maintain prospective cohorts to directly determine incidence. Cross-sectional assays for incidence are also increasingly accepted due to improved performance of new assays and their associated algorithms.[2] However, these assays can misclassify some long-term infected individuals as recent cases.[3] The frequency of such misclassifications on a population level is known as the false recent rate (FRR). The FRR can vary by geographical area, HIV-1 subtype, or presence of ''elite'' or viremic controllers (long-term nonprogressors), and might be affected by host genetic factors, and the extent of ARV use in the area.[1,4] The FRR is a part of the HIV recency algorithm and it, therefore, affects the estimated HIV incidence. The existing uncertainty in estimation of HIV incidence can be partially explained by a lack of local FRR estimates. Applying multiassay algorithms that combine multiple serological assays with available clinical and epidemiological data[5] could reduce FRR, particularly those algorithms that utilize viral load data.[3,6]

In this study, we estimated the FRR in 1,036 HIV-infected treatment-naive individuals from longitudinal observational studies in Botswana sampled between 2004 and 2009. The HIV-positive status of enrolled individuals at baseline was determined by positive HIV antibody tests and detectable HIV-1 RNA (>400 cps/ml). Specimens were collected from ART-naive subjects enrolled in two cohorts, Dikotlana,[7] $n = 725$, and Botsogo,[8] $n = 311$, after 1.5–2 years of follow-up. The Dikotlana cohort[7] was from a prospective, randomized double-blind placebo-controlled longitudinal clinical trial that tested the effectiveness and safety of multivitamins and selenium supplementation in comparison with placebo in 878 HIV-infected ART-naive adults. The Botsogo cohort[8] was from an HIV-1 disease progression observational cohort of 442 HIV-infected, ART-naive adults who did not qualify for ART according to Botswana national guidelines at the

[1]Division of Medical Virology, Faculty of Medicine and Health Sciences, Stellenbosch University, Tygerberg, South Africa.
[2]Botswana Harvard AIDS Institute, Gaborone, Botswana.
[3]National Health Laboratory, Ministry of Health, Gaborone, Botswana.
[4]Harvard T.H. Chan School of Public Health, Boston, Massachusetts.
[5]Florida International University, College of Health and Urban Affairs, Miami, Florida.
[6]National Health Laboratory Services (NHLS), Tygerberg Coastal, South Africa.

Table 1. False Recent Rate for Limiting Antigen-Avidity Assay Cross-Sectional Incidence Assay in HIV-Infected Botswana Patients

Variable	*Cohort 1 (Dikotlana[7])*	*Cohort 2 (Botsogo[8])*	*Total*
Samples	725	311	1,036
Female gender	254 (81.7%)	531 (73.2%)	785 (75.6%)
Age, median (Q1,Q3)	35 (30, 42)	34 (29,42)	35 (30, 42)
CD4 median (Q1,Q3)	396 (302, 526)	392 (311, 515)	394 (302, 524)
HIV RNA, median (Q1,Q3) $\log_{10}$ copies/ml	4.25 (3.54, 4.86)	4.17 (3.33, 4.90)	4.25 (3.51, 4.87)
FRR ODn <1.5	0.64% (2/311)	1.10% (8/725)	0.97% (10/1036)
FRR ODn <1.5 and HIV RNA >1,000 copies/ml	0% (0/311)	0.55% (4/75)	0.39% (4/1,036)

Q1, 25th percentile; Q3, 75th percentile; FRR, false recent rate; ODn, normalized optical density.

time of enrollment. Written informed consent was obtained from all participants, and the study was approved by Harvard School of Public Health's Institutional Review Board and the Health Research Development Committee in Botswana.

Most participants were female (75.6%) and the median age was 35 (IQR 30–42) years at enrollment (Table 1). The median CD4 cell count was 394 cells/mm^3 (IQR 303–524). The median HIV-1 RNA was 4.25 cps/ml (IQR 3.51–4.87). In the limiting antigen (LAg) assay, 10 specimens had optical density units below 1.5, resulting in an FRR of 0.97% (10/1,036; 95% CI 0.46–1.77). Four samples had HIV-1 RNA >1,000 cps/ml, resulting in an adjusted FRR of 0.39% (4/1,036; 95% CI 0.11–0.99).

The HIV recency algorithm that includes the LAg assay and HIV-1 RNA data produced a low FRR in the Botswana population sampled in the mid-2000s. To our knowledge, this is the first report of n LAg-avidity-based FRR for the Botswana population, and it is lower than both the 2% recommended by the WHO Incidence Assays Working Group[9] and previous LAg-avidity-based estimates of the FRR in other settings.[6] Our results support the importance of HIV-1 RNA load being included in the algorithm for estimation of HIV incidence, especially in settings with a large number of individuals on ARV like Botswana.[10]

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Disclosure Statement

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Address correspondence to:
Sikhulile Moyo
Division of Medical Virology
Faculty of Medicine and Health Sciences
Stellenbosch University
Tygerberg 7505
South Africa

E-mail: sikhulilemoyo@gmail.com