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MSM in Bogotá are living with HIV for extended periods without diagnosis or treatment

Maria Cecilia Zea¹, Patricia Olaya², Carol A Reisen¹, and Paul J Poppen¹

¹George Washington University, Washington, DC 20052

²Centro de Análisis Molecular, Bogotá, Colombia

Abstract

We examined recency of infection in serum samples obtained from 69 newly identified HIV-positive cases in a sample of 1000 MSM in Bogotá. HIV antibody avidity assays were performed using the Architect HIV Ag/AB combo. Avidity indices ranged from 0.62 to 1.22, with a cut-off score below 0.80 indicative of recent infection. Two samples were classified as recent, six fell within the gray zone (0.75 to 0.85), and the remaining 61 were considered established infections. Results provided evidence of widespread, long-term, undiagnosed HIV infection, as well as an estimate of one-year incidence at .25 in the population of MSM in Bogotá. This incidence rate is approximately 8.5 times the rate estimated for the general adult population in Colombia. The large proportion of newly diagnosed cases found among individuals with established infections indicates that many MSM in Bogotá are living with HIV for extended periods without being diagnosed and treated. Greater efforts to detect and treat undiagnosed infections are crucial to decrease HIV incidence and increase maximum effectiveness of medical intervention. Given the over-representation of MSM and transgender women in the HIV epidemic in Colombia, such efforts should specifically target this population.

Keywords

HIV; avidity index; recent infection; undiagnosed infection; Colombia; MSM

Introduction

As in other parts of Latin America, HIV in Colombia presents as a concentrated epidemic among men who have sex with men (MSM). In our recent study in Bogotá, we found that half the MSM recruited through respondent-driven sampling reported that they had never been tested for HIV,¹ an alarming finding in light of a prevalence rate of 12.1%.² Although there are additional estimates of prevalence among MSM in Colombia,^{3–6} there is little information about incidence. Indeed, information about incidence is scarce for the general population in Colombia as well. UNAIDS created a model that estimates incidence in generalized epidemics based on prevalence, and with this approach, incidence among adult Colombians (15 to 49 years) was calculated as .0323% in 2013.⁷ A different method that

involves a mathematical model using case reports of detected diagnoses in relation to deaths and stage of disease calculated a similar rate in the general population.⁸

HIV incidence and rates of recent infections are important indicators of the state of an epidemic. Accurate incidence estimates are rare, because of the practical and financial challenges inherent in conducting prospective cohort studies to identify new infections. Therefore, alternative approaches are needed. Bio-marker methods, such as avidity indices of HIV antibodies, are sometimes utilized to characterize recent HIV infections in cross-sectional studies. The potential importance of these methods has been recognized.^{9–16} A WHO Working Group was formed to encourage collaboration and to promote efforts to develop accurate procedures for estimating incidence based on immune responses, as well as to establish guidelines for algorithms for calculating incidence and associated confidence intervals.¹⁷ Although studies have demonstrated the promise of assays to provide indications of recency of infection and incidence,^{9,11–14,16} they have also indicated potentially elevated rates of false identifications of established infections as recent, as well as challenges related to variability among HIV-1 subtypes, among individuals in their immune responses, and among populations in their antibody maturation.^{17,18}

A prominent bio-marker method is based on avidity, the strength of antibody-antigen binding. Avidity has been shown to be low during the early period after transmission (e.g., 6 to 12 months) and to increase until complete antibody maturation occurs.¹⁶ In this study, we explore recency of infection in newly identified HIV cases among MSM in Bogotá, Colombia. We examined serum samples of newly identified cases² and used a fourth generation antibody avidity index to test for recency, a procedure described by Suligoi and colleagues.¹⁶ This procedure has been found to have 91.5% accuracy in identifying recent infections, with sensitivity of 89.4%, specificity of 93.4%, and a false-positive rate of 6.6%.¹⁶

Methods

Participants and serum samples

Participants were recruited using respondent-driven sampling (RDS) for a study on HIV prevalence and sexual risk. RDS is a long chain referral approach that attempts to account for biases due to non-independence, and it is used to recruit hidden populations, such as MSM.^{19,20} The quantitative component of the study (with HIV testing) included a sample of 1000 MSM and transgender women. Eligibility criteria for the study and the pilot included being between the ages of 18 to 49, being born as a biological male, living in Bogotá, and having had sex with a man in the last six months. Although we were not seeking transgender women, we included them when they met eligibility requirements (n=58). Data were collected over ten months in 2011.² In conducting this research, we complied with the Principles of the Ethical Practice of Public Health and received approval of procedures from the George Washington University Internal Review Board. All participants gave informed consent prior to participation in the study.

In addition to responding to a computerized survey, all participants received pre- and post-test counseling and HIV testing with an oral swab (OraQuick Advance Rapid HIV 1/2

Antibody Test). Serum samples were obtained to confirm reactive results from participants who reported not having been previously diagnosed with HIV. We obtained a total of 70 serum samples, although one had insufficient volume to enable analysis. Thus, the final sample for the current analysis was 69; of these, seven were transgender women.

Laboratory methods

Procedures to assess avidity followed those described by Suligoi and colleagues.^{13–15} We used the Architect HIV Ag/AB combo (Abbott Laboratories) with a cutoff score of .80, based on previous research,¹⁶ and confirmed by our findings with control samples. Two aliquots with 1:10 dilutions were used: one dilution was phosphate-buffered saline (PBS), and the other was with 1 M guanidine hydrochloride (G) obtained from Invitrogen catalogue (15502-016). Before processing the diluted samples, they were incubated at 37°C for five minutes. The avidity index (AI) was calculated as $(S/CoG)/(S/CoPBS)$, where S/CoG denotes the Sample/Cutoff G, and S/CoPBS denotes the Sample/Cutoff PBS. As in previous research, we considered 0.80 the cut-off score for recency of infection; to account for error we treated AI between 0.75 and 0.85 as within a gray zone. Thus, we interpreted AI below 0.75 as low avidity and recent infection, and AI above 0.85 as high avidity and established infection.

In addition to following procedures from Suligoi and colleagues^{13–16}, we examined four controls with known time of infection from internal data of the Centro de Análisis Molecular in Bogotá. Two controls had been infected more than 10 years earlier, and two had recent infections: one was acute and one occurred two months earlier. Three tests of avidity were conducted on each of the controls. Table 1 shows the viral loads and the resulting avidity of the controls. Viral load was examined using the m2000 RealTime HIV-1 assay (Abbott Laboratories), an in vitro reverse transcription-polymerase chain reaction (RT-PCR) assay on the automated *m2000* System.

Results

In the sample of 69, the avidity index ranged from 0.62 to 1.22, with a mean and median of 1.00 (S.D. = 0.08). Table 2 shows the AI and viral load for samples characterized as recent infections (6 months or less) and established infections (more than 6 months) infections, as well as those falling within the gray zone. Two samples (2.9%), both from MSM subset, had low avidity and were classified as recent infections. An additional six samples (8.7%) fell within the gray zone for classification; three of these were samples from transgender women. The remaining 61 (88.4%) had high avidity, and therefore were considered to be established infections. Of these, three samples were obtained from transgender women.

Measured viral load ranged from 55 to 455,147 copies per mL. In addition, for calculation purposes, we assigned a viral load of 49 copies per mL to one case with undetectable viral load. Including this value, the mean viral load was 45,509 (S.D. = 85,897) and the median was 13,042. The case with undetected viral load was classified as a recent infection based on Avidity Index. Viral load was below 2,000 in 12 additional samples. Based on the avidity, we classified one of these as falling within the gray zone and the rest as established infections.

In order to calculate an estimate of incidence, we used data collected over ten months, which included 69 usable serum samples. Of these, 2 were classified as recent infections during this period. Extrapolating to a one-year period, we would expect 2.4 recent infections per year. Of the 1000 individuals in the sample, 53 had been previously diagnosed, therefore they were eliminated from the denominator, so that the denominator would reflect the number of people who had the potential to become infected ($1000 - 53 = 947$). Thus, we estimated a one-year incidence rate among MSM in Bogotá at $(2.4/947)$, which is .2534.

Discussion

We found two incident cases and estimated a one-year incidence rate of .25. This rate is approximately 8.5 times the rate estimated for the general adult population in Colombia.^{7,8} This discrepancy is not surprising given the concentration of the epidemic among MSM: in Bogotá prevalence in this group has been estimated at 12.1%² and 15.0%.^{2,6} In comparison, HIV prevalence in the general adult population is .45%.⁷

Because RDS uses a chain-sampling approach, statistical adjustments have been developed to account for dependence among observations.^{19–21} To estimate prevalence in the larger sample, we applied such strategies.² However, in the current paper we had a subsample of 69, and therefore, did not have the continuous chains necessary for this type of adjustment.

Although we are reporting an incidence rate, we recognize that these results should be viewed with caution. As noted above, the development of precise bio-marker methods for estimating incidence remains a work-in-progress.¹⁸ Currently, HIV incidence assays are seen as most appropriate for population-level estimates, which would be most accurate with extremely large samples.^{17,18} Incident assays have been criticized for over-estimating the number of recent infections,^{17,18} which could have occurred in this study. It is also possible, however, that we may have failed to detect incident infections because of the window period associated with the OraQuick Advance Rapid HIV 1 / 2 Antibody test, which we used to determine whether to draw blood.

The relatively low viral load (below 2,000 C/mL) found among some samples classified as established could be in viremic controllers (long-term non-progressors), as defined by Taborda and colleagues²². The criteria defining non-progression are not universal, however, and the observed proportion (17%) exceeds rates typically reported.^{23–26} Without longitudinal indicators of viral load and CD4 counts, we cannot determine whether these individuals are truly long-term non-progressors. It is also possible that some participants did not choose to report their seropositive status, but that they had been previously diagnosed and were currently receiving anti-retroviral therapy.

Results indicated that a large proportion of the newly diagnosed cases were found among individuals with established infections. This finding points to the fact that many MSM in Bogotá are living with HIV for extended periods without being diagnosed and treated. Early detection of HIV is crucial, not only to avert transmission resulting from lack of treatment and high viral loads^{27–30}, but also to improve health outcomes for infected individuals.^{31–33} Greater efforts to detect and treat undiagnosed infections are crucial to decrease HIV

incidence and increase maximum effectiveness of medical intervention. Given the over-representation of MSM and transgender women in the HIV epidemic in Colombia, such efforts should specifically target this population.

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Table 1**Descriptive statistics for control samples (N=4)**

Sample	Time of infection	Viral Load C/mL	Avidity Tests			Results Mean (S.D.)	Interpretation
			Log	1	2	3	
C1	> 10 years	Und	Und	1.22	1.06	1.13	1.14 (0.08) High
C2	> 10 years	Und	Und	1.01	1.01	0.96	0.99 (0.03) High
C3	Acute	1,090,067	6.03	0.34	0.37	0.33	0.35 (0.02) Low
C4	2 months	73,348	4.80	0.56	0.59	0.47	0.54 (0.06) Low

Note: Und= Undetectable

Table 2Avidity Indices and viral loads of the Bogotá samples ($N = 69$).

	Avidity Index	Viral Load	
		C/mL	Log
Low Avidity ($N = 2$)			
1	0.63	Und	Und
2	0.62	6,148	3.79
Gray Zone ($N = 6$)			
1	0.83	2,840	3.45
2	0.84	76,384	4.88
3	0.83	8,717	3.94
4	0.83	1,277	3.11
5	0.83	9,398	3.97
6	0.82	10,879	4.04
Mean	0.83	18,249(28,735)	3.90
High Avidity ($N = 61$)			
Mean	1.00 (0.08)	49,580 (90,232)	4.70

Note: Und= Undetectable