Risk-based Assessment Does Not Distinguish Between Recent and Chronic HIV-1 Infection in Rio de Janeiro, Brazil

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This study investigated the risk factors associated with recent and chronic HIV infections among individual attending a voluntary counseling and testing (VCT) site in Rio de Janeiro, Brazil. In a cross-sectional study, recent HIV infections were detected by the sensitive/less-sensitive test, using Serologic Testing Algorithm for Recent HIV Seroconversion (STARHS) strategy, and compared to chronic HIV infection and HIV negative individuals. Seroincidence was estimated and risk factors associated with recent and chronic infections were assessed using multinomial logistic regression. Among the 7,379 individuals tested between June 2006 and April 2007, the overall prevalence and incidence of HIV infection were 7.5%; and 1.39/100 PY, respectively. In multivariate analysis, having a HIV positive steady partner was a risk factor for recent and for chronic HIV infection for MSM, heterosexual male and women. No differences in risk factors for recent and chronic infections were found between MSM and heterosexual males. Among women, chronic infected individuals were more likely than HIV negatives to be older. Recently HIV infected women were more likely than HIV negatives to be less educated; and more likely than HIV negatives and chronically infected to report having more partners. Routinely used risk-based assessment in testing centers in Brazil lack sensitivity to distinguish between recent and chronic infections, particularly among MSM and heterosexual males. Steady relationships and serosorting may be playing a key role in maintaining the HIV epidemics in Brazil.
Key-Words: STARHS, HIV seroconversion, VCT; Steady partner; HIV; HIV prevention.

Identification of individuals at high risk for HIV infection is of paramount importance for the conduct of studies on preventive strategies and on treatment of recent infections. The ability to differentiate recent from long-standing infection with the Serologic Testing Algorithm for Recent HIV Seroconversion (STARHS) [1] was a major contribution for estimating HIV-1 incidence, providing a simple tool for better understanding the dynamics of the HIV epidemic. STARHS, a two step testing strategy that consists of applying a less sensitive (LS) enzyme-linked immunoassay to a serologically confirmed case, relies on the fact that antibody levels are lower in early HIV infection than in established infections [1]. We conducted a cross sectional analysis to investigate risk factors associated with recent (RI) and chronic (CI) HIV infections using the STARHS strategy in a public voluntary counseling and testing (VCT) site in Rio de Janeiro, Brazil.

Material and Methods

The VCT site is located at Hospital Escola São Francisco de Assis of the Universidade Federal do Rio de Janeiro and provides HIV counseling and testing to approximately 8,000 individuals per year. Data on demographic and risk behaviors are collected through a structured questionnaire that is used in all publicly funded VCT sites in Brazil. De-identified data are entered into a national database. As part of a study on recently acquired HIV-infection, all individuals who sought testing between June 2006 and April 2007 were offered a LS test in case their conventional serology was found to be positive. An informed consent for the performance of the LS assay (the BED Capture EIA [2]) was obtained at the initial visit, prior to collection of blood. Also in the initial visit, a questionnaire about demographics and risk behaviors was applied during the individual counseling. For the present report, de-identified demographic data, risk behaviors and previous diagnoses of sexually transmitted diseases (STDs) were abstracted from the VCT's database. Demographic variables included: sex, age and education (categorized as at least 8 years of formal education or less). Risk behaviors included: number and type of partners (steady versus casual) in the last 12 months; reported HIV-positive steady partner; condom use in the last sexual encounter with a casual partner; condom use with the steady partner; and STDs in the preceding 12 months. Barriers for not using condom with steady and casual partners were grouped into 5 categories: trust, condom-related (cost/access, lack of knowledge, discomfort), inability to negotiate, carelessness, and other. Steady partnership was defined as a sexual relationship lasting at least 12 months; this definition allows more than one simultaneous steady partnership. The annual incidence estimates were obtained using the consensus formula

$$I = \frac{(365/w)N_{inc}}{N_{neg} + (365/w)N_{inc}/2} \times 100$$

and

$$95\%CI = I \pm 1.96 \frac{I}{(\sqrt{N_{inc}})}$$

where I = estimated incidence; w = window period; Ninc = number of recently infected; and Nneg = number of seronegative samples [3]. All analyses were stratified by risk category as men who have sex with men (MSM), heterosexual males, and females.

For univariate analyses, comparisons between RI, CI, and HIV Negative (HN) were made by Chi-square or Fisher's exact tests for categorical variables, and the Kruskal-Wallis test for continuous variables. To assess the relationship between risk factor and outcome, multinomial logistic regression models were fitted using HN as the reference group. Odds ratios and 95% confidence intervals were calculated. Comparisons between RI and CI were made by the Wald test. Stata software (version 9.0; Stata) was used for the analyses.

Results

During the study period, 7,379 individuals were tested for HIV-1 infection. Of these, 851 (11.5%) were MSM, 2,718 (36.8%) were heterosexual males, and 3,810 (51.6%) were heterosexual females. The overall HIV-1 prevalence was 7.5% (553/7,379), and 47 subjects (0.6%) were identified as RI. The overall estimated HIV seroincidence was 1.39 per 100 PY (95%CI 1.19 – 1.59). HIV seroincidence was higher among MSM than heterosexual males and females [6.29 (95%CI 4.87 – 7.69); *vs* 1.20 (95%CI 0.88 – 1.50), and 0.66 (0.47 – 0.85) per 100 PY, respectively, p<.01]. The median number of partners in the preceding 12 months was 3 (IQR 1-6), 2 (IQR 1-4), and 1 (IQR 1-2) for MSM, male heterosexuals and female heterosexuals, respectively.

Among MSM, univariate analysis showed that HN, CI and RI did not differ statistically in terms of age [median 28 (IQR 24 – 38); 29 (24 –36); and 31 (24 – 34) respectively; p=.79]; proportion of individuals who reported not having used condom in the last sexual encounter with a casual partner (72.2, 66.2, and 66.7%; p=.54); history of a STD in the preceding 12 months (10.6, 11.0, and 15.0%; p=.82); having had 4 or more partners in the preceding 12 months (36.6, 41.2, and 35.0; p=.38); and having at least 8 years of formal education (87.7, 82.9, and 99.0%, respectively; p=.06). RI and CI were more likely than HN to report having a HIV-infected partner (20.0, 31.5, and 17.4%, respectively; p =.01). In all groups, the most frequently reported reason for inconsistent condom use with a steady partner was trust: 54.9, 56.1, and 44.4% for HN, CI and RI, respectively. As for reasons for not using condoms with casual partners, carelessness was the most frequently reported reason by HN (29.6%) and RIs (66.7%), whereas condom-related issues were most frequently reported by CIs (27.6%). In multivariate analysis adjusted for education and steady partner's risk, CI were more likely than HN to report having a HIV-infected partner.

Among heterosexual men, in univariate analysis, RI tended to be older than CI and HN [42 (31 – 50); 35 (29 – 44); and 33

(25 – 44) respectively; p<.01]. RI were more likely than CI and HN to have less than 8 years of formal education (46.7, 38.6, and 30.4%, respectively; p=.03). As for risk behaviors, a similar proportion of HN, CI and RI reported not having used condom in the last sexual encounter with a casual partner (77.9, 77.4, and 66.7%, respectively; p=.75). With regards to the number of partners, no differences were found between the three groups: having had at least 4 sexual partners in the preceding 12 months was reported by 27.4, 30.8, and 26.7% of HN, CI and RI, respectively (p=.63). None of the RI reported a history of STD, a finding that did not differ statistically from CI and HN (0.0, 11.4 and 13.4%, respectively; p=.23). The most common reason for not using condoms with the steady partner was trust (60.5, 50.5 and 75.0% for HN, CI and RI, respectively). Condom-related issues were the most commonly reported reasons for not using condoms with casual partners in all groups (34.6, 30.2, and 60.0% for HN, CI and RI, respectively). Being HIV-positive was the most commonly reported partner's risk among RI (71.4%) but not among CI and HN (30.9, and 8.8%, respectively; p<.01). In multivariate analysis controlled for age, education and partner's risk, RI and CI were more likely than HN to report having a HIV-positive partner.

Among women, univariate analyses showed that CI were older than HN and RI [37 (29 – 44); 30 (23 – 41); and 31 (26 – 44); p<.01]. CI and RI reported fewer years of formal education than HN (50.7, 50.0, and 38.1% with < 8 years; p<.01). Rates of inconsistent condom use with casual partners were similar in all 3 groups (77.3, 69.2, and 100.0% for HN, CI and RI, respectively; p=.74), as well as the proportion of women reporting a STD in the preceding 12 months (8.8, 11.5, and 0.0% for HN, CI and RI; p=.30). The most commonly reported reason for not using condom with steady partners was trust (48.8, 51.8, and 55.6% for HN, CI and RI); whereas no consistent pattern was reported for casual partners. Women in the RI group tended to report more sexual partners than those in the CI and HN groups (25.0, 8.1, and 7.2%; p=.05); and were more likely to report having a HIV-infected partner (50.0, 23.2, and 5.9%; p<.01). Multivariate analysis controlled for age, education, number of partners and partner's risk showed that Recent HIV infected women were less educated than HN, more likely to report having had more partners, and to report having a HIV-infected partner. Results of multivariate analyses for all risk categories are shown in Table 1.

Discussion

We previously reported the estimated incidence of recent infections in men and in nonpregnant women using the STARHS algorithm [4,5]. The present results indicate that, on average, the incidence of RI in our setting has declined over time, a trend that remained even after excluding pregnant women from the analysis (data not shown). The higher estimated incidence of RI among MSM compared with heterosexual men and women suggests that the HIV transmission rate remains high within this risk category despite the extensive public health prevention efforts.

Table 1. Adjusted odds ratios (OR) and 95% confidence intervals (95% CI) of recently and chronically infected relative to HIV negative individuals stratified by risk categories.

Characteristic	MSM (n=851)			Male Heterosexual (n=2,718)			Female Heterosexual (n=3,810)		
	Chronically infected (n=206) OR (95% CI)*	Recently infected (n=20) OR (95% CI)	CI vs. RI* p value**	Chronically infected (n=187) OR (95% CI)	Recently infected (n=15) OR (95% CI)	CI vs. RI p value	Chronically infected (n=149) OR (95% CI)	Recently infected (n=12) OR (95% CI)	CI vs. RI p value
Age	-	-	-	1.00 (0.98–1.02)	1.02 (0.96–1.08)	.47	1.02 (1.00–1.04)	0.99 (0.94–1.06)	.40
< 8 yrs of education	1.54 (0.78–3.01)	1.90 (0.20–17.8)	.85	1.20 (0.74–1.95)	1.11 (0.24–5.19)	.92	1.08 (0.65–1.78)	6.03 (11.13–32.18)	<.05
>4 partners in past year	-	-	-	-	-	-	0.95 (0.32–2.55)	12.27 (2.48–60.68)	<.01
Steady partner HIV positive	2.23(1.30–3.81)	1.27 (0.13–11.83)	.59	4.41 (2.62–7.43)	24.48 (4.62–129.78)	.05	3.98 (2.15–7.36)	24.29 (4.92–119.91)	<.01

*CI indicates Chronically infected; RI indicates Recently infected **Wald test p value.

Our results suggest that the behavior-based risk assessment questionnaire that is being used in VCT sites in Brazil lacks sensitivity to distinguish RI from CIs, particularly among MSM and heterosexual men. No particular behavioral pattern was found to be associated with RI in the MSM risk category, when traditional confounders were taken into account. In a similar study conducted at a VCT site in Santos, Brazil, only a history of sex work was independently associated with risk of RI, whereas condom use, number of sexual partners, partner's HIV status and demographic characteristics did not differ between RI and CI [6]. Taken together, these results suggest that the risk assessment questionnaire that is currently used in VCT sites in Brazil may not effectively capture risk behaviors that are presently driving the HIV epidemic.

In a large study using the STAHRS algorithm in samples from 10 US cities, a previous history of urethral gonorrhea was independently associated with risk of RI [7]. In our study, no association was found between previous STD and risk of RI in all risk categories. In fact, individuals with RI reported fewer STDs in all risk categories. Given that having a HIV-infected steady partner was the strongest risk factor for RI, our results suggest that steady relationships may be playing an important role in the HIV epidemics in Brazil.

A trend toward older age of RI was seen among heterosexual men and women, when compared with CI and HN. This tendency was also reported in a population based study conducted in New York City, US [8], and may reflect testing practices among older versus younger men, whereby the former group seeks testing more frequently and are more likely to be diagnosed with RI. On the other hand, the association between RI and fewer years of formal education, a proxy for socio-economic status, in both heterosexual men and women categories is consistent with historical trends in Brazil, indicating that the epidemic continues to move to lower socio-economic strata of the population.

There are several limitations to our study, in particular the specificity of the BED-EIA, which has been reported to yield false positive results in AIDS cases and to overestimate incidence, particularly in settings with high prevalence of subtypes C and A1 [9]. Although we were not able to estimate the bias due to possible inclusion of individuals with AIDS, it is likely to be low, since the vast majority of individuals seeking testing are asymptomatic. Infecting subtypes are unlikely to have influenced our results, since subtypes C and A are rarely encountered in Rio de Janeiro, where subtypes are B and F represent almost the totality of infections [10,11]. The external validity of our results is also open to discussion, given that the study population does not necessarily represent the general population. Thus, the higher estimated incidence among MSM and older heterosexual males and females may be due to the fact that these populations may seek HIV testing more often. In addition, relatively few female sex workers currently seek testing at the Hospital Escola São Francisco de Assis VCT due to the availability of several outreach programs [12].

In conclusion, our study suggests that the structured questionnaire presently used in publicly funded VCT sites in Brazil lacks sensitivity to detect risk factors of recently HIV infected individuals, particularly MSM and heterosexual males. Additionally, our results suggest that steady relationships may be playing a key role in the HIV epidemics in Brazil. Further studies that address risk behaviors in detail are needed for better understanding the Brazilian epidemic and for guiding public health interventions.

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