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Early HIV Infections Among Men Who Have Sex with Men in Five Cities in the United States

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Abstract

We tested blood samples from men who have sex with men (MSM) to detect early HIV infection. Early HIV included both acute (infected past 30 days) and recent (estimated recency past 240 days). Acute infections were defined as screen immunoassay (IA) negative/NAAT-positive or IA-positive/Multispot-negative/NAAT-positive. Recent infections were defined as avidity index cutoff <30 % on an avidity-based IA and, (1) not reporting antiretroviral therapy use or, (2) HIV RNA >150 copies/mL. Of 937 samples, 26 % (244) were HIV-infected and of these 5 % (12) were early. Of early infections, 2 were acute and 10 recent; most (8/12) were among black MSM. Early infection was associated with last partner of black race [adjusted relative risk (ARR) = 4.6, confidence intervals (CI) 1.2–17.3], receptive anal sex at last sex (ARR = 4.3, CI 1.2–15.0), and daily Internet use to meet partners/ friends (ARR = 3.3, CI 1.1–9.7). Expanding prevention and treatment for black MSM will be necessary for reducing incidence in the United States.

Resumen

Utilizamos muestras de sangre de hombres que tienen sexo con hombres (HSH) para detectar infección temprana de VIH. La infección temprana de VIH incluía tanto infecciones agudas (infectado en los 30 días anteriores) como recientes (infectado en los 240 días anteriores). Las infecciones agudas se definieron como: resultados de tamizaje por immunoensayo (IA, por sus siglas en inglés) negativo/NAAT-positivo, o IA-positivo/Multispot-negativo/NAAT-positivo. Las infecciones recientes se definieron como índice de avidez <30 % en un ensayo de avidez y, (1) participante no reporto estar en terapia antiretroviral o, (2) carga viral >150 copias/mL. De las 937 muestras, 26 % (244) estaban infectadas por VIH, y de estas 5 % (12) eran infecciones tempranas. De las infecciones tempranas, 2 eran agudas y 10 recientes; la mayoría (8/12) eran en HSH afroamericanos.Las infecciones recientes estaban asociadas con reportar ultima pareja sexual afroamericana (riesgo relativo ajustado [RRA] = 4.6, intervalo de confianza [IC]:1.2–17.3), sexo anal receptivo en la última relación sexual (RRA = 4.3, IC: 1.2–15.0), y uso diario del Internet para encontrar parejas sexuales/amigos (RRA = 3.3, IC: 1.1–9.7). Para reducir la incidencia de VIH es necesario expandir la prevención y el tratamiento en HSH afroamericanos en los Estados Unidos.

Keywords

HIV; Acute; Early; Recent; MSM; NHBS; United States; African American

Introduction

Identifying early HIV infections in HIV-affected communities is important for several reasons. First, estimating HIV incidence is essential for monitoring the epidemic and assessing the impact of interventions. Second, individuals with recently acquired HIV infection may play a key role for HIV transmission due to high viral loads during the early

stages of HIV infection and to the presence of risk behaviors that may have led to the acquisition of HIV [1, 2]. Describing characteristics of persons with recent infection could help identify factors that may be associated with ongoing HIV transmission and also identify subgroups where HIV acquisition is high, helping to focus HIV prevention programs [3, 4].

To reduce the biases and financial burden of following cohorts to estimate HIV incidence, researchers have developed incidence assays for cross-sectional surveys [3, 4]. However, these assays often overestimate HIV incidence because some long-term infections are classified as early infections. Viral suppression has been shown to be one of the factors that could be associated with this misclassification, and can be both natural or induced by antiretroviral therapy (ART) [5]. Self-report of antiretroviral treatment has been used to exclude patients from being considered recently infected; however, it may be inaccurate. Adding viral load as part of a multi-assay algorithms in cross-sectional surveys has been suggested to improve accuracy in the detection of early infections [6].

Gay, bisexual, and other men who have sex with men (MSM) are disproportionately affected by HIV in the United States [7, 8]. Black MSM have over twice the HIV prevalence of white MSM [7]. The disparity in HIV prevalence is not explained by a higher prevalence of risk behaviors [9]. The Center for Disease Control and Prevention (CDC), National HIV Behavioral Surveillance (NHBS) was initiated in 2003 to monitor HIV-associated behaviors by conducting surveys in populations at high-risk of HIV infection, including MSM. We conducted a pilot study in 2011 to detect early HIV infection in five metropolitan areas (hereafter referred to as cities). Early HIV included both acute (infected in the past 30 days) and recent infections (estimated recency period of 240 days). The objective of the study was to describe the frequency of early HIV infection, identify groups with higher HIV transmission potential that could be targeted for testing and prevention, and generate hypotheses on factors that may contribute to increased HIV transmission.

Methods

MSM were recruited using venue-based, time–space sampling during 2011. Activities included: (1) formative research to identify venues and times to recruit MSM; (2) development of sampling frames of eligible venues and day-time periods; (3) random selection of venues and day-time periods; and (4) recruitment, questionnaire administration, blood collection and HIV testing during sampled events.

Eligibility criteria included being: male, ≥18 years of age, a resident of the selected cities, reporting sex with another man during lifetime, and able to provide informed consent. Trained interviewers used handheld computers to administer a standardized anonymous questionnaire. Anonymous HIV testing was offered to all participants regardless of self-reported HIV sero-status. Whole blood was collected for either conventional laboratory testing or rapid testing in the field followed by laboratory confirmation. HIV test results were returned to participants in person or by telephone.

The pilot study to detect early HIV infection was conducted in Baltimore, MD, Washington, DC, Miami, FL, Los Angeles, CA, and Denver, CO. A tube of EDTA-whole blood or frozen

plasma was sent to the CDC laboratory overnight for processing and testing. At CDC, all specimens were screened with a 4th generation immunoassay (IA), GS HIV Ag/Ab Combo (BioRad Laboratories, Redmond, WA). Repeatedly reactive specimens were tested with Multispot HIV-1/HIV-2 rapid test (BioRad Laboratories). Nucleic Acid Amplification Test (NAAT) by APTIMA HIV-1 RNA qualitative assay (Gen-Probe Incorporated, San Diego, CA) was performed to resolve discordant test results and on all specimens that screened negative on IA. For HIV-positive specimens (IA-positive and Multispot-positive), we used an avidity-based modified GS HIV-1/HIV-2 Plus O IA to identify recent infections [10]. Those identified as recent were further tested for HIV RNA concentration using the Abbott M2000 Real-Time HIV-1 assay (Abbott Laboratories, Abbott Park, IL). Acute infections were defined as NAAT-positive and either IA-negative or IA-positive (Ag/Ab Combo) and Multispot-negative. Recent infections were defined as an avidity index cutoff <30 % (estimated recency period of 240 days for subtype B) (Michele Owen, personal communication) and (1) not reporting use of antiretroviral therapy for their HIV infection or (2) not virally suppressed (defined as HIV RNA concentration >150 copies/mL). It has been documented that the avidity assay (similar to other assays available to detect recent infections), misclassifies individuals with long-term infections as recent [11]. We used self-reported current use of antiretroviral therapy and undetectable HIV viral loads to exclude long-term infections from those classified as recent. activities for the 2011 cycle of NHBS were reviewed by the Institutional Review Boards (IRB) for each participating city and approved by CDC.

Data Analysis

This was a pilot study and the sample size varied by site. Our analysis was considered exploratory and for hypothesis generation. We assessed the associations between early infection (including both acute and recent) and selected demographic and behavioral variables in order to identify subgroups with higher percent of early infections and to identify potential risk factors for HIV acquisition. Since we wanted to focus on factors associated with HIV acquisition, we excluded long-term infections (HIV serology positive not determined as recent by the avidity-based assay) from the bivariate analysis and compared individuals with early infection to HIV-uninfected MSM. The variables selected included basic demographic characteristics such as age, race, income and education and selected behaviors that have been associated in previous research with HIV risk, such as injection and non-injection drug use, use of the internet to meet sex partners, number of sex partners, exchange of sex for drugs or money, receptive anal sex, condom use and partner characteristics such as partner type, race/ethnicity, age, and HIV status (only available for last partner).

Participants were included in this analysis if they had a complete, reliable survey questionnaire and reported ≥1 male sex partner in the past 12 months. Variables associated with the outcome in bivariate analysis were considered for the multivariable model and retained if associated with the outcome at $\alpha = 0.10$ based on the Wald Chi square test. Generalized estimating equations using a robust variance estimate and assuming a Poisson model was used to estimate adjusted relative risks (ARR) and 95 % confidence intervals

(CI). *P* values ≤0.05 were considered statistically significant. SAS software was used for all analyses.

Results

Of 992 specimens received, 937 satisfied the analysis criteria. A total of 26 % (244 men) were HIV-infected. Of the HIV-infected men, 49 % (120) were self-reported positive. Among self-reported positives, 78 % (93) were on ART.

There were two acute infections, one IA negative/NAAT-positive and one IA positive/Multispot negative/NAAT-positive. Among 242 antibody-positive specimens, 22 were identified as recent by the avidity-based assay. Nine of the 22 recent infections were among self-reported positive on ART and 13 among self-reported negative MSM. Eight of the nine self-reported positive MSM reported being diagnosed before 2011, with year of diagnosis ranging from 1989 to 2011. The nine self-reported positive MSM on ART were considered long-term infections misclassified as recent and excluded from the risk factor analysis. Furthermore, three self-reported negative individuals identified as recent by the avidity-based assay were virally suppressed, considered long-term infections and also excluded from the risk factor analyses. Overall, after removing the individuals reported to be on ART and virally suppressed, there were a total of 12 early infections (12/244, 5 %), two acute and 10 recent.

Of early infections, most were among black men (8/12) and from the city of Baltimore (7/12) (Table 1). Variables associated with early infection in bivariate analysis (Table 2) were black race of participant, being recruited in Baltimore, having a last sex partner of black race, having had receptive anal sex at last sexual intercourse and using the internet daily to meet sex partners or socialize. Other behaviors in the past 12 months were not associated with early infection. In multivariable analysis adjusting for city the following variables remained associated with early HIV infection: having a last sex partner of black race (ARR 4.6; CI 1.2–17.3), having had receptive anal sex at last sexual intercourse (ARR 4.3, 95 % CI 1.2–15.0) and using the Internet daily to meet sex partners or socialize (ARR 3.3, 95 % CI 1.1–9.7).

Discussion

Identifying where and among whom new infections are occurring is key for HIV prevention. In this pilot study, we found a high prevalence of HIV infection and a percentage of MSM with acute and recent HIV infection similar to what has been reported in other studies [12]. Although most early infections were among black MSM, after controlling for the effects of other covariates in the model, black race of the last sexual partner but not black race of participants, along with receptive anal sex, and daily use of the Internet to meet partners or socialize were independently associated with having early HIV infection.

Although black MSM have been found to be either less likely or equally likely than white MSM to engage in high-risk behaviors [13], HIV disparities between black and white MSM persist. Our study suggests that black MSM may have increased risk of HIV infection because they tend to have sexual networks that carry a higher prevalence of HIV, such as

male partners of the same race/ethnicity (4). High HIV prevalence and incidence within the sexual networks of black MSM could in part explain the observed racial/ethnic disparities. Previous research has suggested that sexual networks of black MSM are smaller and potentially more highly interconnected than other groups. Once HIV enters one part of such tightly connected network, it is likely to spread and maintain a high prevalence of HIV [13]. Studies across the US have found that black MSM are 11 times as likely to have black partners and 50 % more likely to have older partners compared with other MSM [14]. A study in Los Angeles, found that the odds of HIV infection among black MSM decreased by 20 % after adjusting in multivariate analyses for older sexual partners and having anal sex with black partners [15].

The higher prevalence of HIV among black MSM, lower awareness of HIV-positive status [16], lower access to antiretroviral therapy and lower likelihood of being virally suppressed [17], in concert with more in-group sexual partnering [13], places black MSM at a greater risk of HIV infection despite similar or lower risk behavior than other MSM. It has been suggested that black MSM with two condomless anal intercourse partners have as much as a 40 % risk of HIV infection compared with a 20 % risk for white MSM with the same number of partners [18].

We found that receptive anal sex at last sex was associated with early HIV infection, probably explained by the higher per act transmission probability of receptive anal sex and the imperfect protection from condoms. Receptive anal sex is the riskiest type of sex for acquiring HIV and estimates for the risk of HIV acquisition are eight times higher for receptive (138 per 10,000 exposures) than for insertive sex (11 per 10,000 exposures) [19]. While condoms can reduce the risk of HIV transmission, they do not eliminate the risk and are not always used consistently and correctly. Consistent condom use has been shown to be 70 % effective in preventing HIV acquisition during anal sex [20].

Daily Internet use to meet sex partners or socialize with gay men may be increasing the risk of HIV acquisition. The association between early infection and daily Internet use was especially evident among black MSM (data not shown). A 2006 meta-analysis reported that on average 40 % of MSM use the Internet to meet sex partners and 30 % had sex with partners met online [21]. Also, several risk behaviors have been associated with online sex-seeking, including multiple sex partners, anal sex without condoms, higher risk sexual practices such as fisting and group sex and drug use before and during sex [22].

Most early HIV infections detected in this study were from Baltimore. Data from prior NHBS surveys among MSM in Baltimore have shown high rates of HIV infection and unawareness of infection, with disproportionate concentration of HIV among black MSM [23]. Baltimore has consistently had the highest prevalence of HIV among MSM across cities participating in NHBS [24–26]. Using NHBS data on all participants from 2011, HIV prevalence among MSM in Baltimore was 41 %, while only 31 % of HIV-positive MSM were aware of their infection [16]. For the other cities participating in this pilot HIV prevalence among MSM in 2011 was lower than in Baltimore while awareness was higher (Denver 15 and 77 %; Los Angeles, 17 and 77 %; Miami 23 and 80 %, Washington DC, 13 and 77 %) [16]. The high proportion of recent infections found in the current study supports

indications of a persistent and dynamic HIV epidemic among black MSM in Baltimore and helps to validate prior reports of undiagnosed HIV infection. Despite local efforts to intensify prevention and coordinate the response to the HIV epidemic, HIV transmission remains high among MSM in Baltimore.

The misclassification by the avidity assay of long-term infections as recent infections among individuals on ART has been reported previously and has also been documented as a limitation of other available assays used to detect recent infection [11]. Future studies that incorporate determination of early infection should collect information on ART use and if possible, include HIV viral load testing to correct for potential misclassification by laboratory assays.

The analysis presented here is subject to several limitations. This is a pilot study, the sample size per city was small and there were only a few early infections, limiting the statistical power to identify risk factors for early HIV infection. These data are cross-sectional and therefore we cannot infer causal relationships between self-reported behaviors and early HIV. Data are not weighted to account for the complex sampling methodology. MSM were recruited from MSM-identified venues in five cities with high AIDS burden with varying sample sizes and results may not be generalizable to all MSM. We were able to identify long term infections misclassified as recent based on the ART history of participants and viral load measurements. However, if treatment was started soon after infection, individuals with recent infection could have been erroneously classified as long-term infections.

The detection of early infections as part of ongoing behavioral surveillance among MSM can contribute to the understanding of key factors for continued HIV transmission and acquisition. Future research can help better understand the role of sexual networks for HIV transmission among MSM, and the factors that mediate the relationship between Internet-based sexual partnering and HIV risk behavior. Efforts to reduce HIV racial disparities should ensure that HIV-negative black MSM have access to prevention interventions such as PrEP and HIV-positive black MSM are linked to care, have access to effective treatment regimens and adherence and risk reduction counselling. These efforts are key to reduce onward HIV transmission among black MSM sexual networks.

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Table 1

HIV prevalence and percent of infections that were early infections among MSM in the 5-city pilot study, National HIV Behavioral Surveillance, 2011

	Total screened No.	HIV infected No.	HIV prevalence %	Percent of infections that were early (recent or acute) %
Age (in years)				
18–24	262	53	20.2	7.5
25–29	201	44	21.9	9.1
30+	474	147	31.0	2.8
Racial/Ethnicity				
Black	344	146	42.4	5.6
White	304	44	14.5	4.5
Hispanic	202	36	17.8	5.6
Other[a]	85	16	18.8	0.0
Income				
≤$19,999	336	103	30.7	3.9
$20,000–39,999	245	62	25.3	4.9
≥$40,000	335	66	19.7	6.2
Education				
High school or less	342	109	31.9	6.5
Some college or higher	594	134	22.6	3.8
City				
Baltimore	333	140	42.0	5.1
Denver	157	11	7.0	9.1
Los Angeles	320	75	23.4	1.3
Miami	32	6	18.8	16.7
Washington DC	95	12	12.6	16.7
Most recent HIV test[b]				
Never	68	18	26.5	5.6
>12 months ago	216	40	18.5	2.6
≤12 months	529	65	12.3	15.6
All	937	244	26.0	5.0

Percents may not add to 100 % due to missing values

[a]Other races include American Indian, Alaska Native, Asian, Native Hawaiiian, other Pacific Islander, and mixed race

[b]Excluded self-reported positive (n = 120)

Table 2

Risk factors for early HIV infection among men who have sex with men, 5-city pilot study, National HIV Behavioral Surveillance, 2011

	Total at risk[a] No.	Percent with early infection among those at risk[a]		
		%	Relative risk 95 % CI	Adjusted relative risk 95 % CI
Racial/ethnicity[b]				
Black	206	3.9	4.8 (1.5, 16.0)	1.1 (0.3, 5.3)
Other	499	0.8	1.0	1.0
Age group (years)				
18–24	213	1.9	1.2 (0.4, 3.8)	
25+	492	1.6	1.0	N.A.
Education				
High school or less	240	2.9	2.7 (0.9, 8.5)	
Some college or higher	465	1.1	1.0	N.A.
City[b]				
Baltimore	200	3.5	3.5 (1.1, 11.0)	1.6 (0.4, 6.3)
Other	505	1.0	1.0	1.0
Past 12 months behaviors				
Number of male partners—12 months				
1	137	0.7	0.3 (0.04, 2.9)	
2–4	281	1.8	0.9 (0.3, 2.8)	
5+	287	2.1	1.0	N.A.
Stimulant use				
Yes	220	0.9	0.4 (0.1, 2.0)	
No	483	2.1	1.0	N.A.
Characteristics of last sex partner				
Partner age				
Younger	287	1.7	2.1 (0.2, 17.4)	N.A.
Older	298	2.0	2.4 (0.3, 19.5)	
Same Age	118	0.8	1.0	
Partner type				
Main	312	1.6	0.9 (0.3, 3.2)	
Casual	393	1.8	1.0	N.A.
Partner race/ethnicity[b]				
Black	209	4.3	6.4 (1.7, 24.0)	4.6 (1.2, 17.3)
Other	492	0.6	1.0	1.0
Receptive anal sex at last sex[b]				
Yes	262	3.1	3.1 (0.9, 10.3)	4.3 (1.2, 15.0)
No	446	0.9	1.0	1.0
Receptive anal sex without a condom				

	Total at risk[a] No.	Percent with early infection among those at risk[a]		
		%	Relative risk 95 % CI	Adjusted relative risk 95 % CI
Yes	122	2.5	2.0 (0.5, 7.5)	
No	584	1.7	1.0	N.A.
Frequency of Internet use to meet sex partners[b]				
≥Once a day	140	4.3	3.7 (1.1, 12.6)	3.3 (1.1, 9.7)
<Once a day to never	563	1.1	1.0	1.0
Total	708			

N/A non-applicable

[a]We excluded long-term infections (HIV serology positive not determined as recent by the avidity-based assay) and compared individuals with early infection to HIV-uninfected MSM

[b]Considered for multivariate model