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Gonorrhea and Chlamydia Testing Rates of HIV-Infected Men: Low Despite Guidelines

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Abstract

Objectives—Screening HIV-infected men for gonorrhea (GC) and *Chlamydia* (CT) may decrease HIV transmission and reduce the incidence of pelvic inflammatory disease in female partners. This study determined GC/CT testing rates in a clinical HIV cohort before and after 2003 when the U.S. Centers for Disease Control and Prevention issued guidelines for GC/CT screening.

Methods—First GC/CT testing episodes were identified for all men enrolling in a Baltimore HIV clinic 1999–2007. Multivariate Cox and logistic regression were used to assess clinical and demographic factors associated with being tested and with having a positive result.

Results—Among 1110 men, the rate of GC/CT testing upon clinic enrollment increased from 4.0% prior to 2003 to 16.5% afterward, and the rate of ever being tested increased from 34.2% to 49.1% ($P < 0.001$ for both comparisons). Among men with same sex contact, 10% of first testing episodes included extragenital sites. Among the 342 men ever-tested, 5.2% had positive results on first testing. Predictors of testing included enrolling after 2003, younger age, frequent visits, and black race. Predictors of a positive test result included CD4 count ≥ 200 cells/mm³ and younger age.

Conclusions—GC/CT testing rates among men increased substantially after the 2003 guidelines but remain low. Disseminating existing evidence for GC/CT screening and promoting operational interventions to facilitate it are warranted.

Keywords

health service research; gonorrhea; Chlamydia; screening; HIV secondary prevention

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INTRODUCTION

Screening HIV-infected men for *Neisseria gonorrhoeae* (GC) and *Chlamydia trachomatis* (CT) may decrease HIV transmission and reduce sequelae such as pelvic inflammatory disease in female partners.[1–3] Reducing genital fluid HIV viral loads and prompting opportunities for sexual behavior counseling are mechanisms whereby GC/CT screening and treatment may reduce secondary HIV transmission.[2,4] In June 2003, the U.S. Centers for Disease Control and Prevention recommended considering GC/CT screening upon enrollment into care and at least annually thereafter for all sexually active HIV-infected persons.[5] Such screening should include oral and rectal (extragenital) sites when sexual history indicates relevance.

While the prevalence of active GC and/or CT among patients of HIV-clinics has ranged from 2.5 to 11%, and incidence may be as high as 15 per 100 person years,[1,4,6–10] uptake of screening recommendations in clinical practice may be poor.[11] This may be especially true for men, since GC/CT screening in women often occurs simultaneously with cervical cancer screening. We determined rates and predictors of testing and rates and predictors of test positivity before and after June 2003 among men in a large HIV cohort in Baltimore, Maryland.

METHODS

This analysis is based on data collected in the Johns Hopkins HIV Clinical Cohort (JHHCC) study, which offers enrollment to all persons initiating longitudinal HIV care at the Johns Hopkins Hospital HIV clinic.[12] Comprehensive data collection is based on abstraction from medical records and electronic laboratory databases. Since its inception in 1989, >99% of clinic patients have joined the study. All male subjects who first enrolled between 1999 and 2007 and were enrolled for ≥ 3 months were included in this analysis. Maintenance of the JHHCC and use of its contents for analysis were approved by the Institutional Review Board of the Johns Hopkins School of Medicine.

All GC and/or CT tests performed from 90 days prior to clinical enrollment through either the last visit or March 31, 2008 were identified. Tests included nucleic acid amplification tests (NAATs) and cultures from genital, oral, and rectal sites. Tests upon enrollment were defined as occurring ≤ 90 days before or after enrollment. Additional clinical variables for analysis included enrollment date; yearly number of provider visits; age; race; HIV-risk factor(s); and use of highly active antiretroviral therapy (HAART), defined as any combination of ≥ 3 medications representing ≥ 2 antiretroviral classes.

Cox regression was used to assess factors associated with ever being tested for GC/CT. The validity of proportional hazards assumptions was confirmed through visual inspection of log log plots and the calculation of Schoenfeld residuals. All covariates associated with testing by $P \leq 0.2$ in univariable analyses were examined in a multivariable model. Among all men tested, multivariable logistic regression was used to assess factors associated with a positive result. P values < 0.05 were considered statistically significant. STATA 10.0 (College Station, Texas) was used for all analyses.

RESULTS

Among 1110 men enrolling in HIV continuity care from 1999–2007, 75% were 30–49 years-old upon enrollment and 78% were African American. Forty-three percent reported high-risk heterosexual contact, 41% injection drug use (IDU), and 33% same sex contact (MSM) as HIV risk factors (Table). Thirty-eight percent (423 men) had GC and/or CT tests performed on at least one body site on at least one occasion during a median of 42 months

(interquartile range: 18–71) of follow-up. First testing episodes occurred at a median of 23 months (6–45) after enrollment, predominantly included both GC and CT (92%), and used NAAT (95%) rather than culture.

The rate of testing upon enrollment increased from 4.0% among men enrolling January 1999 – June 2003 to 16.5% among men after June 2003; the rate of ever being tested increased from 34.2% prior to June 2003 to 49.1% afterward (Fisher's exact $P < 0.001$ for both comparisons). In univariable and multivariable Cox regressions, ever being tested for GC/CT was associated with care occurring after June 2003, attending a mean of ≥ 4 visits/year, younger age, and African-American race (Table). HIV risk factors, enrollment CD4 count and HIV RNA level, and ever-using HAART were not associated with GC/CT testing. Of the 368 MSM in the cohort, 142 (39%) were ever-tested for GC/CT. Fourteen (10%) of first testing episodes in these men included extragenital (rectal and/or pharyngeal) sites. Seven extragenital site testing episodes occurred after June 2003.

Among 81 men tested upon enrollment, 5 (6.2%) were positive for GC (4 men) or CT (1 man). Among the 342 men first tested after enrollment, 17 (5.0%) were positive on first testing (9 with GC, 8 with CT, and none with dual infections). Of 46 men ≥ 50 years old who were tested, none were positive. One MSM was positive at an extragenital site (rectal infection with a lymphogranuloma venereum *Chlamydia* serotype) on a test performed 13 months after enrollment.

In multivariable analysis, younger age at time of testing (adjusted odds ratio (AOR) for age < 30 vs. age ≥ 40 years, 5.70 [95% CI: 1.54, 21.10] and for age 30–39 vs. ≥ 40 years, 4.55 [1.51, 13.74]) and CD4 count ≥ 200 cells/mm³ at time of testing (AOR vs. CD4 count < 200 cells/mm³, 8.73 [1.14, 66.61]) were associated with a positive result. A sensitivity analysis using enrollment CD4 count rather than CD4 at time of testing found an AOR for CD4 ≥ 200 cells/mm³ of 3.74 [1.03, 13.57]. Testing after June 2003, mean yearly visits, race, HIV risk factors, HIV RNA level and use of HAART at time of testing were not associated with a positive test result.

DISCUSSION

Our findings show that a significant increase in GC/CT testing occurred after the 2003 guidelines were published. To our knowledge, ours is the first study to estimate this change in testing rate over time. Despite the increase, less than 17% of men enrolling after 2003 were tested upon enrollment into care and less than 50% were ever tested. Only 10% of first testing episodes in MSM included rectal and/or oral sites.

A recent study of HIV clinics in 6 US cities found similar evidence of low GC/CT screening rates among MSM; the annual GC/CT screening rate for the calendar year 2005 was approximately 21%.[11] Our study identifies that there is a low rate of enrollment screening among non-MSM men and confirms the finding that testing rates are low among MSM. The low rate of extragenital site testing among MSM may be particularly problematic as a majority of incident GC/CT in this population may be missed when only urethral testing is performed.[4,6–7]

The low rate of GC/CT testing in men contrasts rates of other HIV-related health maintenance practices such as rates of *P. jirovecii* and *M. avium* prophylaxis which were $> 85\%$ among men during 1999–2007 in our clinic (data not shown). The reason(s) for this contrast are not clear. HIV providers may be unaware or unconvinced by the literature supporting widespread GC/CT screening in men or dissuaded by sexually transmitted infection (STI) associated stigma or by the types of specimens to be collected. Providers at our clinic are generally aware of high STI rates in Baltimore.[13–14] Four negative clinical

trials versus only one positive trial of community-wide GC/CT treatment to prevent HIV transmission in Africa may have convinced some providers that screening is not useful.[15–19]

HIV providers may be overwhelmed by the required number of routine health maintenance tasks. Operational interventions such as pop-up reminders and standing orders are potential solutions which have shown effectiveness in pneumococcal vaccination programs.[20–22] Sixty-six percent of women enrolled 1996–2006 in our cohort were tested at least once,[23] with this higher rate for women potentially reflecting the effect of engagement in cervical cancer screening.

Providers may test sparingly, but they may be targeting their testing at men who give histories of recent high-risk exposures. Our finding that high CD4 count was associated with a positive result but not with being tested provides preliminary evidence that persons with high CD4 count could represent an overlooked risk group. This conclusion must be taken with caution given the low number of positive tests in our sample, but a plausible mechanism exists in that men with higher CD4 counts may be more likely to engage in high-risk sex. High CD4 was found to be an independent risk factor for GC/CT in a Los Angeles HIV-infected MSM cohort but not in a New England cohort.[4,9] Our results indicate younger HIV-infected men are more likely to have GC/CT as well as to be tested for it, although 5 infections (23%) occurred in men over 40 years old. These age-related findings are similar among women in our cohort.[23]

Emerging literature supporting screening includes evidence that brief, clinically-feasible counseling by providers can reduce high-risk sexual behaviors.[24–25] Targeting such counseling toward men with incident GC/CT should help reduce HIV transmission. Also, screening high risk heterosexual men from the general population for GC/CT has demonstrated favorable cost-effectiveness when the reduction of GC/CT related sequelae among female partners is considered.[3]

In April 2009, enrollment GC/CT screening was added to the U.S. Department of Health and Human Services HIV/AIDS Bureau's list of clinical performance measures.[26] Continued government (Ryan White Program) funding to clinics may depend on meeting performance standards. Future studies will be needed to determine if this increases screening rates.

A limitation of our study is that we cannot distinguish screening tests from symptom-prompted tests. We suspect that the majority of tests within 90 days of enrollment were performed for screening. While an increase in symptom-prompted testing after 2003 could explain some of the 2.7 fold increase in the rate of ever-being tested, this does not affect the conclusion that the overall screening rate since 2003 is low, and, at best, less than 50%. Some of our patients may have been tested at other locations (e.g. city public health clinics), however these data are generally not available to our providers when deciding whether to screen. Our data reflect a single HIV clinic with a high prevalence of African Americans and IDUs. Nonetheless our data may be representative of many urban HIV clinics.

In summary, this analysis demonstrates low GC/CT enrollment testing and overall testing of HIV-infected men despite a response to national guidelines. Future studies should examine the efficacy and cost-effectiveness of increasing screening of all men and/or of certain high-risk groups as well as barriers to increasing screening. Meanwhile, efforts may be focused on better disseminating the existing evidence and on operational interventions which facilitate screening in clinical practice.

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Table
Factors Associated with Ever Being Tested for GC/CT

	N (%)	Univariable HR (95% CI) of Ever Being Tested	P	Multivariable AHR (95% CI) of Ever Being Tested
Time Period of Enrollment				
1999 – June 2003	819 (73.8)	1.00 (Ref)	---	1.00 (Ref)
July 2003 – 2007	291 (26.2)	2.65 (2.11, 3.33)	<0.001	2.70 (2.15, 3.40)
Mean Visits / Year				
<4	389 (35.1)	1.00 (Ref)	---	1.00 (Ref)
≥4	721 (65.0)	1.51 (1.23, 1.84)	<0.001	1.55 (1.27, 1.91)
Age in Years				
Median (IQR)	41 (35–46)	---	---	---
18 – 29	105 (9.5)	2.01 (1.36, 2.97)	<0.001	2.42 (1.63, 3.59)
30 – 39	372 (33.5)	1.13 (0.80, 1.57)	0.49	1.39 (0.99, 1.95)
40 – 49	465 (41.9)	1.37 (0.99, 1.90)	0.05	1.53 (1.11, 2.12)
≥50	168 (15.1)	1.00 (Ref)	---	1.00 (Ref)
Race / Ethnicity				
African American	861 (77.6)	1.31 (1.02, 1.67)	0.03	1.31 (1.03, 1.67)
White	212 (19.1)	1.00 (Ref)	---	1.00 (Ref)
Other	37 (3.3)	<i>a</i>	---	<i>a</i>
HIV Risk Factor HET^b				
Yes	473 (42.6)	1.09 (0.90, 1.32)	0.37	---
No	637 (57.4)	1.00 (Ref)	---	---
HIV Risk Factor IDU^b				
Yes	453 (40.8)	0.93 (0.76, 1.13)	0.45	---
No	657 (59.2)	1.00 (Ref)	---	---
HIV Risk Factor MSM^b				
Yes	368 (33.2)	1.11 (0.91, 1.36)	0.31	---
No	742 (66.9)	1.00 (Ref)	---	---
Enrollment CD4 Count				
<200 cells/mm ³	476 (42.9)	1.00 (Ref)	---	---
≥200	634 (57.1)	0.96 (0.79, 1.16)	0.66	---
Enrollment HIV RNA				
<1,000 copies/ml	256 (23.1)	1.00 (Ref)	---	---
1,000 – 99,999	528 (47.6)	1.01 (0.79, 1.30)	0.91	---
≥100,000	326 (29.4)	1.13 (0.87, 1.48)	0.36	---
Initiated HAART				
Ever	927 (83.5)	1.08 (0.82, 1.43)	0.58	---
Never	183 (16.5)	1.00 (Ref)	---	---

NOTE. Values expressed as number (percent) unless otherwise noted. Enrollment HIV RNA was missing for 9 men.

^aThe racial category “other” was combined with “white” for univariable and multivariable Cox regression analysis.

^b Reporting more than one HIV risk factor was allowed.

HR indicates hazard ratio; AHR, adjusted hazard ratio; Ref, reference; IQR, interquartile range; IDU, injection drug user; MSM, men who have sex with men; HET, heterosexual transmission risk.