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Disparities in herpes simplex virus type 2 infection between black and white men who have sex with men in Atlanta, GA

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Summary

Background—HIV disproportionately affects black men who have sex with men, and herpes simplex virus type 2 is known to increase acquisition of HIV. However, data on racial disparities in herpes simplex virus type 2 prevalence and risk factors are limited among men who have sex with men in the United States.

Methods—InvolveMENT was a cohort study of black and white HIV-negative men who have sex with men in Atlanta, GA. Univariate and multivariate cross-sectional associations with herpes simplex virus type 2 seroprevalence were assessed among 455 HIV-negative men who have sex with men for demographic, behavioral, and social determinant risk factors using logistic regression.

Results—Seroprevalence of herpes simplex virus type 2 was 23% (48/211) for black and 16% (38/244) for white men who have sex with men ($p = 0.05$). Education, poverty, drug/alcohol use, incarceration, circumcision, unprotected anal intercourse, and condom use were not associated with herpes simplex virus type 2. In multivariate analyses, black race for those ≤ 25 years, but not >25 years, and number of sexual partners were significantly associated.

Conclusions—Young black men who have sex with men are disproportionately affected by herpes simplex virus type 2, which may contribute to disparities in HIV acquisition. An extensive assessment of risk factors did not explain this disparity in herpes simplex virus type 2 infection suggesting differences in susceptibility or partner characteristics.

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Conflict of interest

The authors declare no conflict of interest.

Keywords

Herpes simplex virus type 2; men who have sex with men; HIV disparities

Introduction

Men who have sex with men (MSM) are at greatest risk of HIV infection in the United States, with incidence rates comparable to some regions in Sub-Saharan Africa.¹ CDC's National HIV Behavioral Surveillance system estimated in 2008 that non-Hispanic black MSM had the highest prevalence of HIV (28%), followed by Hispanics (18%) and white MSM (16%).² Reasons for stark racial disparities in HIV are complex and not fully understood. Contributors to racial disparities likely include social determinant risk factors (e.g. poverty, access to health care, etc.) and sexual network risk; however, differences in individual behavioral risk do not contribute.³ In order to design effective HIV prevention interventions for MSM and reduce disparities, there is need for increased clarity surrounding racial disparities in HIV, and it is helpful to understand the contribution of all putative risk factors.

Many studies have provided evidence that sexually transmitted infections (STIs) increase acquisition of HIV,⁴ and one putative contributor to disparities in HIV acquisition is higher rates of STI among black MSM. Herpes simplex virus type 2 (HSV-2) is a common STI worldwide and primary cause of genital ulcer disease.⁵ HSV-2 and HIV have similar methods of transmission, and co-infection is very common. HSV-2 can independently enhance the risk of acquiring HIV and has been identified as an important biological predictor of HIV acquisition in the general population and among MSM, specifically.⁶⁻⁸ Increased mucosal susceptibility to HIV infection in the setting of HSV-2 can be a direct effect of epithelial disruption by ulcers, due to subclinical reactivation, or to persistent mucosal immune activation after healing of an ulcer lesion.⁹

In the US, non-Hispanic blacks have the highest life-time seroprevalence (41.8%) of HSV-2 with prevalence nearly four times that of non-Hispanic whites (11.3%).¹⁰ Although a racial disparity in HSV-2 among MSM is suspected, there is no clear evidence. It is possible that if a racial disparity exists, it could contribute to racial disparities in HIV acquisition among MSM. Therefore, the aim of this analysis was to estimate the seroprevalence of HSV-2 in a cohort of black and white MSM in Atlanta, GA, and to examine demographic, behavioral, and social determinant risk associations with HSV-2 serostatus.

Methods

The InvolveMENT study was a longitudinal cohort study of HIV-negative black and white MSM in Atlanta, GA, designed to examine individual, dyadic, and community level factors that may contribute to disparities in HIV and STI. A full description of the study recruitment and methodology has been previously published.¹¹ Briefly, MSM aged 18–39 years were recruited from the Atlanta community primarily using time-space venue sampling.² Facebook was included as a virtual 'venue' in the venue sampling frame.¹² Eligible participants self-identified as black or white MSM, reported sex with another man in the

previous 3 months, not being in a mutually monogamous relationship, could complete survey instruments in English, lived in the Atlanta metropolitan area, and had no plans to relocate in the subsequent 2 years. Men who self-identified as Hispanic or of other/mixed race were not enrolled. At the baseline visit, all participants were tested for HIV and completed a detailed computer-assisted self-interview (CASI) questionnaire to evaluate demographic, individual, dyadic, and community level HIV risk factors. A specimen repository was established in conjunction with the study enabling retrospective analyses of biologic specimens. The Emory University Institutional Review Board approved the study.

HSV-2 serostatus was determined from the baseline study visit for 455 of 560 HIV-negative MSM with available serum specimens enrolled in the study between July 2010 and September 2012. HSV-2 serostatus was evaluated on stored serum specimens using HerpesSelect HSV-2 type specific assay (Focus Diagnostics). Per manufacturer insert, index values >1.10 were considered positive for HSV-2.

The InvolveMENT database was queried for demographic factors including self-reported race, age, and education level. Age was further dichotomised at ≤ 25 years and >25 years for some analyses. Participants were queried about the number of oral and anal sexual partners in the last 12 months and whether they participated in any unprotected anal intercourse (UAI) in the past six months. Condom use was defined as whether or not the participant had used a condom at any time in the past 12 months. Other covariates examined included reported history of any form of physical or sexual child abuse, any history of incarceration, history of alcohol use, history of non-injection drug use, self-reported circumcision status, employment status, poverty as defined by 2011 Federal Poverty Guidelines, health insurance status, whether the participant identified as 'gay' or bisexual, and any reported sildenafil use in the last 12 months.

First, prevalence of HSV-2 and demographic, behavioral, and social determinant risk factors were calculated and compared for black and white MSM using *t*-test and Chi square statistical tests for continuous and categorical variables, respectively. Each variable was then entered into bivariate logistic regression to evaluate crude associations with HSV-2 infection. Statistically significant factors (p value < 0.1) and biologically important indicators were included in a multivariate logistic regression model of HSV-2 infection. An interaction term between age and race was considered in a separate model to examine heterogeneity in the racial difference in HSV-2 status between MSM ≤ 25 and >25 years old. Statistical analyses were performed using SAS 9.3.

Results

Demographic and behavioral characteristics of 455 HIV-negative MSM included in this analysis are presented in Table 1. Forty-six percent (221/455) self-identified as black/African-American. White MSM reported higher levels of education (56% vs. 33% for college; $p < 0.001$), had lower prevalence of poverty (13% vs. 30%; $p = 0.001$), and were more likely to have health insurance (77% vs. 53%; $p < 0.001$) than black MSM. White MSM were significantly more likely than black MSM to identify as homosexual or gay (92% vs. 78%; $p < .001$). White MSM were more likely to report using non-prescription

drugs in the last 12 months than black MSM (52% vs. 28%; $p < 0.001$), and sildenafil use was more common among white MSM (18% vs. 3%; $p < 0.001$). White MSM were more likely to be circumcised (93% vs. 85%; $p = 0.01$) and reported greater numbers of male sexual partners in the past 12 months than black MSM (11 vs. 8; $p = 0.02$).

The overall seroprevalence of HSV-2 was 19%, and black MSM were more likely to have HSV-2 infection than white MSM (23% vs. 16%; $p = 0.05$) (Table 1). When stratifying by age, this difference in HSV-2 seroprevalence was only significant for MSM ≤ 25 years (21% vs. 10%; $p = 0.003$), but not for MSM > 25 years (23% vs. 20%; $p = 0.6$). Table 2 presents univariate and multivariate associations with HSV-2 serostatus. For every year increase in age, the odds of being infected with HSV-2 increased by 5.0% ($p = 0.003$). The odds of HSV-2 infection were increased with higher numbers of male sex partners (OR 1.02 per partner increase; $p = 0.04$). There were no significant associations between HSV-2 serostatus and education, employment status, lack of health insurance, poverty, UAI, condom use, circumcision, drug use, or alcohol use. In the adjusted model, race (aOR 2.3; $p = 0.005$), age (aOR 1.1; $p = 0.005$), and number of male sexual partners in the past 12 months (aOR 1.03; $p = 0.007$) were independently associated with HSV-2 infection.

In a multivariable model that further included an interaction term for age and race (data not shown), the overall test of interaction between race and age was statistically significant ($\beta = -0.10$; $p = 0.04$). When examining the race-HSV-2 association among levels of age, black race was significantly associated with HSV-2 infection only among MSM ≤ 25 years (aOR = 5.3; $p = 0.002$). There was no significant association between race and HSV-2 infection among older MSM.

Discussion

We demonstrate a high prevalence of HSV-2 infection among black and white MSM at risk of HIV infection in the US, and further show marked racial disparities in HSV-2 infection among HIV-negative MSM ≤ 25 years. Our data support other studies showing age and the number of sexual partners to be independently associated with HSV-2 infection, as seen in the general population and among MSM specifically.^{8,13–17} Other individual behavioral risk factors (e.g. UAI, drug use, condom use, etc.) and social determinant risk factors (e.g. poverty, health insurance status, etc.) examined were not associated with HSV-2.

Overall seroprevalence of HSV-2 in our study was similar to age-specific national estimates in the general population and among MSM in the US. Recent estimates of HSV-2 seroprevalence in the general population from the National Health and Nutrition Examination Survey (NHANES) showed marked racial disparities that increased with age; an average of 17.1% of non-Hispanic blacks vs. 3.5% of non-Hispanic whites aged 14–29 years and of 57.4% of non-Hispanic blacks vs. 16.5% of non-Hispanic whites aged 30–49 years are estimated to have HSV-2 infection.¹⁰ Seroprevalence among MSM was 18.4% in an earlier study from NHANES,⁵ although this study did not report data stratified by race or age. It is interesting to note that while black, HIV-negative MSM had higher prevalence of HSV-2 than white MSM in our study, disparities were more marked in younger men. This implies that drivers of racial disparities in HSV-2 among HIV-negative MSM may be

different than the general population. On the other hand, by including only HIV-negative MSM in our study we may have introduced selection bias for lower-risk, older men who are less likely to have HSV-2 infection, and diluted the racial disparity among older MSM.

Our data support other studies showing age and the number of sexual partners to be independently associated with HSV-2 infection, as seen in the general population and among MSM specifically.^{13,15} Data from an HIV vaccine clinical trial among MSM showed circumcision status was associated with a borderline significant reduction in HSV-2 seropositivity.⁸ More research is needed to understand the contribution of circumcision to HSV-2 acquisition as we did not see an association in our study. We also did not find an association between reported condom use in the last 6 months and HSV-2 infection; however, we did not assess consistency of condom use for all sexual acts in this analysis. Some studies have shown a reduction in HSV-2 incidence with increased condom use among heterosexuals;¹⁸ therefore, further examination of condom use among MSM as a prevention method for HSV-2 infection should be pursued.

Race/ethnicity, number of sexual partners, and age have consistently emerged as risk factors for HSV-2 among MSM in US and international settings.^{8,17} Our univariate analysis showed a significant association between child physical and/or sexual abuse and HSV-2. High prevalence of child sexual and/or physical abuse has previously been reported among MSM,¹⁹ and a prior study of MSM in China found that a history of sexual abuse was an independent predictor of HSV-2 infection.²⁰ Since child abuse was not associated with HSV-2 in multivariable models in our study, this could indicate that the association between child abuse and HSV-2 was mediated by recent sexual behaviors. In our study, there was no association between alcohol or drug use and HSV-2 status as has been reported for heterosexual men in the US.¹⁴

Reasons for disparities in STI are multifactorial and complex. Social determinants of health including racism, higher poverty rates, higher rates of incarceration, higher rates of unemployment, lower education levels, and lower health insurance coverage among black Americans all operate to influence the epidemiologic context (i.e. sexual networks, individual risk behavior, etc.) and increase rates of STI.²¹ None of the social determinants examined in this study were associated with HSV-2 infection. However, our study focused on individual risk factors and did not examine sexual networks or neighborhood level determinants, which could explain the lack of associations. Therefore, a better understanding of how social determinants shape STI risk and how these factors should best be measured in epidemiologic studies are necessary.

This analysis is limited by our moderate sample size, and metrics generated from HIV-negative MSM in Atlanta are not generalisable to the broader MSM population. We excluded MSM in monogamous relationships, which also limits generalisability of our results. This cross-sectional study was only able to examine prevalent and not incident cases of HSV-2 infection, and our results are based on the assumption that recent behavior is indicative of behavior prior to HSV-2 infection, which could be inaccurate. It is also possible that there was underreporting of high-risk sexual behaviors like UAI and drug use, which may have obscured the association of these behaviors with HSV-2 infection. Finally,

there is evidence that use of a higher index-value cut-off for the HerpesSelect assay improves the positive predictive value of the assay.²² Unfortunately, the index value data was no longer available for a substantial number of assays run for this study, so some men may be misclassified as HSV-2-positive in our analyses.

In conclusion, the exact role of HSV-2 in shaping racial disparities in HIV acquisition among MSM in the US is yet to be determined. This is particularly salient for young, black MSM who share a high burden of HSV-2 and HIV. Our data support traditional risk factors for HSV-2 infection (e.g. age, number of sexual partners) in our cohort, but did not identify any associations with social determinants of health. Further studies, including genetic and biologic studies of the interaction between incident HSV-2 and HIV and partnership-level analyses, demand more attention in explaining HSV-2 disparities between black and white MSM.

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Table 1

Demographic and behavioral characteristics of black and white HIV-negative MSM in the InvolveMENT cohort.

Variables	Black n (%) N=211	White n (%) N=244	p Value
HSV-2 prevalence	48/211 (23)	38/244 (16)	0.05
Age in years (mean, std dev)	25.6 (5.4)	28.1 (6.0)	<.0001
Uninsured (now)	97/206 (47)	56/242 (23)	<.0001
Poverty ^a	48/160 (30)	29/223 (13)	<.0001
Education	70 (33)	135 (56)	<.0001
College, post graduate, or professional school			
Some college, Associate's degree, and/or technical school	89 (42)	86 (35)	
High school or GED	46 (22)	29 (9)	
Some high school	6 (3)	0 (0)	
Unemployed (now)	52/210 (25)	42/244 (17)	0.048
Alcohol (12 mo)	197/210 (94)	236/244 (97)	0.1
Uncircumcised	29/195 (15)	17/228 (7)	0.01
Child abuse	91/211 (51)	85/244 (48)	0.07
Gay identity	165/211 (78)	224/244 (92)	<.0001
Number of sexual partners (12 mo) (mean, std dev)	8 (10)	11 (11)	0.02
Sildenafil use (12 mo)	6/203 (3)	39/235 (18)	<.0001
Arrested (12 mo)	26/211 (12)	23/244 (9)	0.3
Condom use (12 mo)	182/209 (87)	193/244 (79)	0.1
Unprotected anal intercourse (6 mo)	70/221 (33)	100/243 (41)	0.08
Drug use (12 mo)	58/209 (28)	127/243 (52)	<.0001

HSV-2: Herpes simplex virus type 2; MSM: men who have sex with men.

^a77 participants were missing data on income and were excluded from these calculations.

Table 2

Associations between HSV-2 serostatus and demographic and behavioral characteristics of HIV-negative MSM in the InvolveMENT cohort.

Variables	OR	95% CI	aOR	95% CI
Black race	1.6	1.0–2.6	2.3	1.3–4.1
Age (per 1 year increase)	1.05	1.02–1.09	1.1	1.02–1.12
Uninsured (now)	1.2	0.7–2.0	–	–
Poverty	1.4	0.8–2.5	–	–
Education			–	–
College or more vs. some high school	1.8	0.1–2.8		
Some college, Associate's degree, and/or technical school vs. some high school	1.0	0.2–4.9		
High school or GED vs. some high school	1.2	0.1–4.3		
Unemployed (now)	0.8	0.4–1.4	–	–
Alcohol (12 mo)	0.7	0.3–2.1	–	–
Uncircumcised	1.8	0.9–3.5	–	–
Child abuse (lifetime)	1.6	1.0–2.5	1.5	0.84–2.56
Gay identity	1.1	0.5–2.1	–	–
Number of sexual partners (12 mo)	1.02	1.001–1.04	1.03	1.01–1.05
Sildenafil use (12 mo)	1.6	0.8–3.3	–	–
Arrested (12 mo)	0.6	0.2–1.4	–	–
Condom use (12 mo)	1.5	0.8–3.0	–	–
Unprotected anal intercourse (6 mo)	1.1	0.8–2.2	1.1	0.6–2.0
Drug use (12 mo)	1.1	0.7–1.7	–	–

HSV-2: Herpes simplex virus type 2; MSM: men who have sex with men.