HHS Public Access

Author manuscript

J Clin Virol. Author manuscript; available in PMC 2017 July 01.

Published in final edited form as:

J Clin Virol. 2016 July ; 80: 93–97. doi:10.1016/j.jcv.2016.05.003.

Parallel declines in HIV and hepatitis C virus prevalence, but not in herpes simplex virus type 2 infection: a 10-year, serial cross-sectional study in an inner-city emergency department

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Abstract

Background—The Johns Hopkins Hospital Emergency Department (JHHED) has served as an observational window on the HIV epidemic in a socioeconomically depressed, urban population. We previously reported that HIV incidence among JHHED patients is decreasing and that prevalence has declined from 11.4% in 2003 to 5.6% in 2013.

Objectives—This study sought to observe temporal trends in hepatitis C virus (HCV) and herpes simplex virus type 2 (HSV-2) seroprevalence, which are surrogate markers for parenteral and sexual risk behavior, respectively.

Study Design—Identity unlinked-serosurveys were conducted over 6–8 weeks in the adult JHHED in 2003, 2007, and 2013. Excess sera from 10,274 patients, previously tested for HIV, were assayed for HSV-2 and HCV antibodies.

Results—Overall HCV seroprevalence declined steadily from 22.0% in 2003 to 13.8% in 2013 (P_{trend}<0.01), and was significant by all gender and race strata. Overall HSV-2 prevalence declined from 55.3% in 2003 to 50.0% in 2013 (P_{trend}<0.01), but was non-significant after adjustment for demographics. Among HIV+ individuals <45 years of age, there was a significant decrease in the proportion of individuals with HCV co-infection [without HSV-2] (P_{trend}=0.02) from 2003 to

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Presentation:

This work was presented in-part at the 2015 *World STI & HIV Congress of the International Society for Sexually Transmitted Diseases* in Brisbane, Australia.

CONFLICT OF INTEREST

Competing Interests:

The authors declare no conflicts of interest.

Ethical Approval:

The study was approved by the Johns Hopkins School of Medicine IRB.

2013, however, there was an increase in individuals with HSV-2 co-infection [without HCV] (P_{trend}<0.01).

Discussion—Little change in age-specific HSV-2 prevalence suggests the decrease in HIV prevalence was likely not associated with changes in sexual risk behavior. In addition to clinical interventions, strategies to address sexual health disparities and continued parenteral harm-reduction efforts are needed to further drive the decline in HIV.

Keywords

HIV; hepatitis C; HCV; herpes; HSV-2; emergency department

BACKGROUND

Urban emergency departments (EDs) serve as primary health care facilities for millions of underserved populations [1], providing a window into the state of public health within the local community. Pioneered by the Johns Hopkins Hospital Emergency Department (JHHED) in Baltimore City, ED-based identity-unlinked serosurveys have provided sentinel observations regarding HIV epidemiology since the late 1980s [2–10]. Most recently, the JHHED noted a two-fold reduction in HIV prevalence from 11.4% in 2003 to 5.6% in 2013 [9]. Although increases in HIV viral suppression during this period correlated with observed declines in HIV incidence estimates [9], changes in sexual or parenteral risk behavior may have also contributed to this waning epidemic.

Herpes simplex virus type 2 (HSV-2) infection is a surrogate marker for risky lifetime sexual behavior and has a biologic role in sexual HIV transmission [11–14]. Urban settings have higher levels of HSV-2 seroprevalence compared to the national prevalence (15.7%) [15–18]. HIV infection is also spread by injection drug use, and an excellent marker of parenteral risk behavior is hepatitis C virus (HCV) infection [19]. There is interest in expanding ED-based HIV screening and linkage-to-care (LTC) programs to now include HCV screening, for which curative therapy now exists [20–27].

OBJECTIVES

This study assessed trends in HIV, HCV and HSV-2 seroepidemiology among patients in the JHHED to: (1) characterize the local burden of disease, and (2) explore potential changes in parenteral and sexual risk behavior during a waning HIV epidemic.

STUDY DESIGN

Study Population

An identity-unlinked serosurvey was conducted during a 6 to 8-week period in 2003, 2007 and 2013 at the adult JHHED in Baltimore, Maryland. The protocol has been described elsewhere [2–4, 8, 9]. Briefly, eligible patients were ≥ 18 years of age, required blood drawn for a medical reason, and had matched chart review data recorded in real-time. Excess sera were collected and assigned a unique study ID—individuals with repeat ED visits were excluded. All patient identifiers were irretrievably stripped from the study database prior to

initiating laboratory testing. This study was approved by the Johns Hopkins School of Medicine Institutional Review Board (IRB).

Laboratory Testing

HIV and HSV-2 testing was performed as previously described [8, 9, 17]. HCV serostatus was determined by the GENEDIA HCV 3.0 ELISA (Green Cross Medical) in 2003 & 2013, and the Ortho HCV 3.0 ELISA (Ortho Clinical Diagnostics) in 2007 [29].

Statistical Analyses

Temporal trends by study year were examined using the Cochran-Armitage test. Prevalence ratios (PR) for seropositivity were determined by Poisson regression with robust variance estimation. Adjusted prevalence ratios (aPRs) were calculated from multivariate models including age, gender, race, and co-infection status.

RESULTS

The study included 10,274 individuals (Table 1). There were unadjusted declines in total HIV, HCV, and HSV-2 prevalence by study year (P_{trend}<0.05; Figure 1). After stratification by race and gender, the temporal age-adjusted decline in HIV prevalence was only significant among black males and black females (P_{trend}<0.01; Table S1), while age-adjusted temporal declines in HCV prevalence were observed for all race-gender strata (P_{trend}<0.05; Table S1). There were no age-adjusted temporal declines in HSV-2 prevalence for any race-gender strata (Table S1).

There were differential reductions in prevalence estimates between 2003 and 2013 among various age-groups (Figure 2). For white females, HIV and HSV-2 prevalence did not significantly decline among any age group, however, a 58% reduction in HCV prevalence was observed among the 25–44 age group (PR=0.42; 95%CI=0.26–0.69; Figure 2A,B). For white males, there was a 93% reduction in HIV prevalence among the 25–34 age-group (PR=0.07; 95%CI=0.01–0.58; Figure 2D), a 41% reduction in HCV prevalence among the 35–54 age group (PR=0.59; 95%CI=0.43–0.81; Figure 2E), and a 42% reduction in HSV-2 prevalence among the 35–44 age group (PR=0.58; 95%CI=0.35–0.94; Figure 2F).

For black females among the 25–44 age group, there was a 69% and 71% decline in HIV prevalence (PR=0.31; 95%CI=0.21–0.46; Figure 2G) and HCV prevalence (PR=0.29; 95%CI=0.20–0.42; Figure 2H), respectively. There was also a 17% decrease in HSV-2 prevalence among the 25–34 age group of black females (PR=0.83; 95%CI=0.73–0.94; Figure 2I). For black males among the 35–54 age group, there was a 61% and 52% decline in HIV prevalence (PR=0.39; 95%CI=0.30–0.51; Figure 2E) and HCV prevalence (PR=0.48; 95%CI=0.41–0.58; Figure 2K), respectively. There was also a 39% decline in HCV prevalence among the 25–34 age group of black males (PR=0.61; 95%CI=0.53–0.70; Figure 2K).

Between 2003 and 2013, there was a 21% reduction in HCV prevalence (aPR=0.79; 95%CI=0.67–0.93) and no change in HSV-2 prevalence among HIV positive individuals (Table 3). Among HIV positive individuals <45 years of age, there were decreasing temporal

trends in HCV/HSV-2 co-infection and HCV infection [without HSV-2] (P_{trend}<0.05), however, there was an increase in HSV-2 infection [without HCV] (P_{trend}<0.05; Figure 3). These temporal trends remained significant after adjustment for demographics. In 2013, HCV infection [without HSV-2] was associated with HIV infection among individuals >45 years of age (aPR=8.49; 95%CI=4.12–17.56), but not among individuals <45 years of age (aPR=1.99; 95%CI=0.48–8.21; Table S2).

Figure S1 illustrates a higher and earlier peak prevalence of HSV-2 among HIV positive individuals compared to HIV negative individuals.

DISCUSSION

This study characterizes HIV, HCV and HSV-2 seroepidemiology during the evolution of a waning HIV epidemic among an inner-city population. Reductions in HCV prevalence were observed in this population, and were most pronounced among black men who were most at-risk for HIV infection. The reduction in HIV/HCV co-infection [without HSV-2] among adults <45 years of age suggests a decrease in parenteral risk behavior, and this hypothesis is supported by local studies of people who inject drugs and the scale-up of harm-reduction efforts [29–33]. However, an aging-cohort effect was also observed for HIV and HCV infection, with notable declines among older black populations, suggestive of an increase in mortality [34, 35]. Nonetheless, the continued high prevalence of HIV and HCV among patients attending the JHHED supports the utility of ED-based screening and LTC programming.

Additionally, these results highlight the sexual health disparities of this population. The black population and HIV-infected persons were disproportionately infected with HSV-2, and minimal temporal declines were observed. Most notable was the high prevalence of HSV-2 among black women, which consistently reached >80% by age 35. The rise in HIV/HSV-2 co-infection [without HCV infection] among individuals <45 years and early age of HSV-2 acquisition in this study is concerning. These data emphasize the need for early and effective control programs for sexually transmitted diseases among inner-city minorities and young adults.

There were limitations to this study. Changes in ED attendance by key populations may have affected our results. Patients were not systematically interviewed for risk behavior, and temporal inferences were solely based on biomarker data that require additional confirmation. Furthermore, the study was limited to a single-site, and results may not be generalizable to other populations. However, the temporal trends observed in this report are compatible with previous serological studies [13, 16, 18, 36–38].

In addition to observed increases in patients on antiretroviral therapy in this ED population [9], reductions in parenteral risk may have contributed to the waning HIV epidemic and prevalence in HCV in this population. Given the biologic synergism of HIV/HSV-2 co-infection and minimal changes in age-specific HSV-2 prevalence, the observed decline in HIV incidence was likely not associated with changes in sexual risk behavior. In order to

further drive the decline of HIV, strategies to reduce sexual risk behavior and continued parenteral risk-reduction efforts are needed to supplement therapeutic interventions.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

Funding:

This work was supported by the Division of Intramural Research and extramural support [K01AI100681] from the National Institute of Allergy and Infectious Diseases.

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Highlights

- Emergency departments can serve as key venues for HIV, HCV, & HSV-2 surveillance.
- There were minimal declines in age-specific HSV-2 prevalence, unlike for HIV & HCV.
- Prevalence of HIV/HCV co-infection [without HSV-2] decreased in persons <45 years.
- Prevalence of HIV/HSV-2 co-infection [without HCV] increased in persons <45 years.
- Gender and racial disparities were persistent throughout the study period.

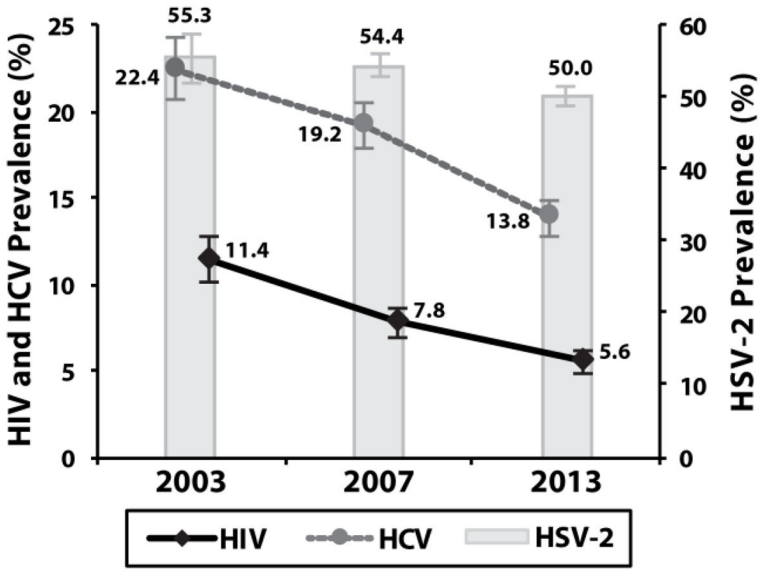

Figure 1. HIV, HCV and HSV-2 seroprevalence in the overall study population

Error bars represent 95% confidence intervals.

Note: 20 individuals had missing HCV data and 23 had missing HSV-2 data.

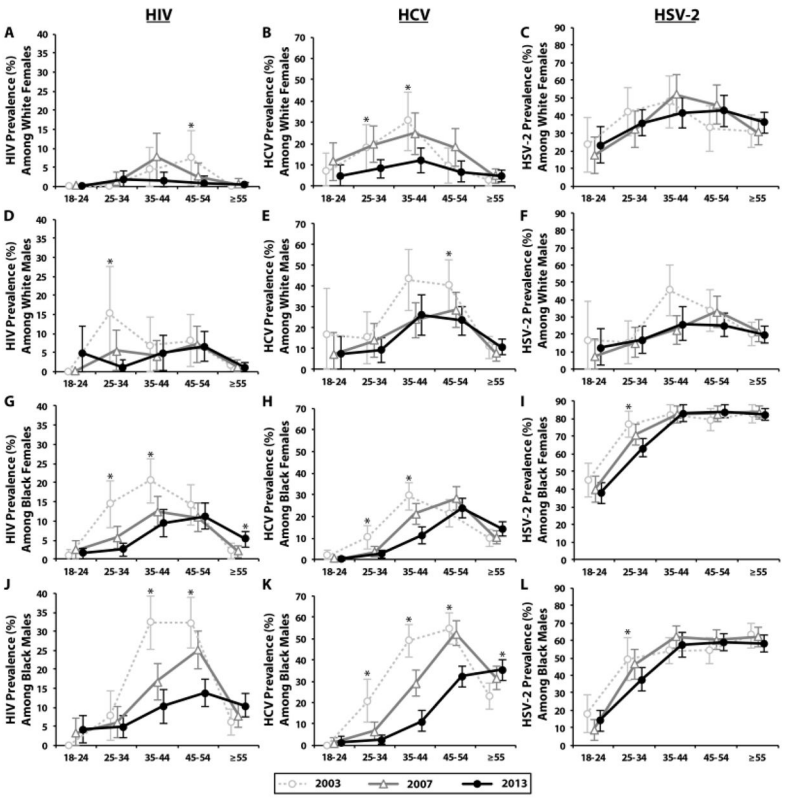

Figure 2. Temporal trends in age-specific HIV, HCV and HSV-2 seroprevalence by race and gender

Error bars represent 95% confidence intervals (excluded if prevalence was 0%).

* Denotes a significant linear trend from 2003 to 2013 ($P<0.05$).

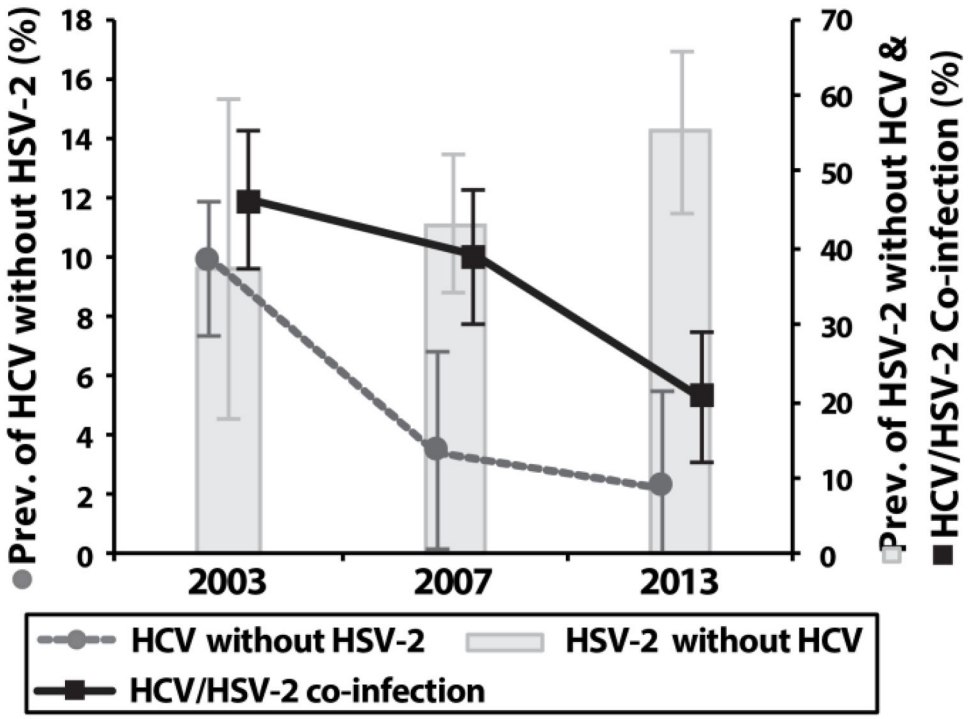

Figure 3. Temporal trends in HCV infection, HSV-2 infection, and HCV/HSV-2 co-infection among HIV-positive individuals <45 years of age

Error bars represent 95% confidence intervals

Table 1

Study demographics.

Characteristic	Study Year, %		
	2003	2007	2013
Gender			
Female	54.5	54.0	55.0
Male	45.5	46.0	45.0
Race			
White	26.4	26.9	29.4
Black	69.0	67.3	63.1
Other	4.6	5.9	7.6
Age			
18–24	9.8	10.5	11.3
25–34	14.0	16.7	19.4
35–44	22.2	20.1	15.3
45–54	22.3	23.2	21.6
≥55	31.7	28.8	32.3
Total, no.	2,144	3,417	4,713

Note: 5 individuals had missing age data and 4 had missing gender data.

Table 2

Reduction in HCV prevalence but not HSV-2 prevalence among HIV positive individuals.

Study Year	HCV Co-infection		HSV-2 Coinfection	
	N (% Pos.)	aPR (95% CI)	N (% Pos.)	aPR (95% CI)
2003	228 (59.6)	**(ref)**	228 (79.8)	**(ref)**
2007	265 (53.6)	0.89 (0.77–1.04)	265 (79.6)	1.02 (0.94–1.11)
2013	262 (48.1)	**0.79 (0.67–0.93)**	258 (78.3)	1.01 (0.92–1.10)

Adjusted prevalence ratios (aPR) were calculated from a multivariate model that included HCV/HSV-2 co-infection, age group, gender, and race. Prevalence in 2003 was the reference group, and aPRs with a $P<0.05$ are shown in bold. N represents the number of individuals analyzed.