Journal of Clinical Virology 74 (2016) 4–7

Contents lists available at ScienceDirect

Journal of Clinical Virology

journal homepage: www.elsevier.com/locate/jcv

Short communication

Herpes simplex virus seroprevalence and seroconversion among active duty US air force members with HIV infection

Jared A. Cohen [a], Amanda Sellers [b], T.S. Sunil [b], Peter E. Matthews [c], Jason F. Okulicz [d,*]

[a] San Antonio Military Medical Center, Department of Internal Medicine, JBSA Fort Sam Houston, TX, United States
[b] Institute for Health Disparities Research, University of Texas at San Antonio, San Antonio, TX, United States
[c] Mike O'Callaghan Federal Medical Center, Infectious Disease Service, Nellis AFB, NV, United States
[d] San Antonio Military Medical Center, Infectious Disease Service, JBSA Fort Sam Houston, TX, United States

ARTICLE INFO

Article history:
Received 4 September 2015
Received in revised form 4 November 2015
Accepted 6 November 2015

Keywords:
Human immunodeficiency virus
Herpes simplex virus
Genital herpes
Sexually transmitted infections

ABSTRACT

Background: Herpes simplex virus (HSV) infection is associated with an increased risk of both HIV transmission and acquisition. We evaluated longitudinal HSV serology and sexually transmitted infections (STIs) among active duty US Air Force (USAF) members with HIV infection.
Methods: USAF members diagnosed with HIV between 1996 and 2012 were included and divided into 2 groups: 1996–2004 ($n = 131$) and 2005–2012 ($n = 266$). HSV-1 and -2 serology was evaluated at HIV diagnosis. Longitudinal HSV-1 and -2 serology and ICD-9 codes for HSV and non-HSV STIs were also examined for those with ≥1 year of follow-up.
Results: Patients were most commonly Caucasian (44.2%) or African American (43.4%) men with a median age of 28 years at HIV diagnosis. HSV-2 seroprevalence at HIV diagnosis decreased from the period of 1996–2004 (48.8%) to 2005–2012 (30.1%; $P < 0.01$). Odds of HSV-2 seropositivity was significantly greater for non-Caucasians (OR 2.19, 95% CI 1.33–3.60) and for HIV diagnosis between 1996 and 2004 (OR 2.06, 95% CI 1.29–3.27), with a trend observed for those age >30 years at HIV diagnosis (OR 1.73, 95% CI 0.94–3.18). A total of 81 (20.4%) patients developed STIs by ICD-9 codes, including 24 (6.1%) new genital herpes diagnoses, during a median follow-up of 4.6 years. HSV-2 seroconversion occurred in 33 of 253 (13.0%) with an incidence rate of 5.07 per 100 person-years (95% CI 4.76–5.37).
Conclusion: Although HSV-2 seroprevalence at HIV diagnosis decreased over time, high-risk sexual behaviors were ongoing as evidenced by the high proportion of new STI diagnoses and HSV-2 seroconversions. Continued education to reduce risk behaviors is warranted to prevent acquisition and transmission of STIs in HIV-infected persons.

Published by Elsevier B.V.

1. Introduction

Herpes simplex virus type 2 (HSV-2) plays an important role in the dynamics of human immunodeficiency virus (HIV) infection. HSV-2 enhances HIV acquisition through genital ulceration, which provides a portal of entry for HIV, and upregulates activated immune cells associated with HSV-2 infection, which may increase the number of immune targets for HIV infection [1]. Subclinical genital erosions in the setting of HSV-2 infection are also thought to facilitate HIV transmission by promoting HIV shedding in the genital tract [2–4]. Studies have demonstrated the clinical significance of HSV in the epidemiology of HIV infection. For example, HSV-2 seropositive individuals had a 2-fold greater risk of HIV acquisition and transmission in prospective studies, even in those without clinical HSV disease [5,6]. Among HIV-infected individuals, ongoing high-risk sexual behavior has important public health implications due to potential transmission of HIV, HSV, and other sexually transmitted infections (STIs).

HSV co-infection represents a challenge for HIV prevention due to the high prevalence of genital herpes among HIV-infected populations worldwide. The most effective method of evaluating HSV prevalence is by use of serosurveys, since the majority of infections are subclinical and case reporting underestimates the true burden of HSV disease [7,8]. HSV-2 seroprevalence among HIV-infected individuals varies with geographic, social and economic characteristics with cohort reports ranging from 30 to 70% in the US and Europe and 50–90% in Africa [7,9–14]. According to National Health and Nutrition Examination Survey (NHANES) data, HSV seroprevalence in the US general population has shown a 7% decline in HSV-1

* Corresponding author at: San Antonio Military Medical Center, 3551 Roger Brooke Drive, Fort Sam Houston, TX 78234, United States. Fax: +1 210 916 5900.
E-mail address: jason.f.okulicz.mil@mail.mil (J.F. Okulicz).

http://dx.doi.org/10.1016/j.jcv.2015.11.012
1386-6532/Published by Elsevier B.V.

Table 1
Baseline characteristics at HIV diagnosis.

Characteristic	All	Year of HIV diagnosis		*P* value
		1996–2004	2005–2012	
Patients (n)	397	131 (33.0)	266 (67.0)	–
Gender, male	390 (98.2)	128 (97.7)	262 (98.5)	0.58
Race/ethnicity				
Caucasian	150 (44.2)	58 (44.3)	92 (44.2)	0.52
African, American	147 (43.4)	62 (47.3)	85 (40.9)	
Hispanic	27 (8)	8 (6.1)	19 (9.1)	
Other	15 (4.5)	3 (2.3)	12 (5.8)	
Median age at HIV diagnosis (years)	283 (24–35)	30 (26–37)	26 (23–34)	<0.05
Age at HIV diagnosis (years)				<0.05
	18–24	117 (29.5)	23 (17.6)	94 (35.3)
	25–30	124 (31.2)	43 (32.8)	81 (30.5)
	31–40	113 (28.5)	53 (40.5)	60 (22.6)
	41+	43 (10.8)	12 (9.2)	31 (11.7)
Rank group				
Enlisted	349 (87.9)	113 (86.3)	236 (88.7)	0.48
Officer	48 (12.1)	18 (13.7)	30 (11.3)	
Median CD4 count at HIV diagnosis (cells/uL)	520 (387–670)	543 (399–694)	510 (378–665)	0.39
Median viral load at HIV diagnosis (log_{10} copies/mL)	4.4 (3.8–4.9)	4.2 (3.4–4.8)	4.4 (3.9–4.9)	0.18
Median time from last negative to first positive HIV test (months)	17.7 (10.7–25.7)	18.9 (11.7–36.0)	17.5 (10.2–24.9)	0.38

All data expressed as number, (%) or median, (interquartile range).

between 2005 and 2010 compared to 1999–2004 and no significant change in HSV-2 [15]. However, longitudinal studies of HSV seroprevalence in HIV-infected populations are limited.

2. Objective

Longitudinal HSV-1 and -2 seroprevalence was evaluated in active duty US Air Force (USAF) members diagnosed with HIV infection between 1996 and 2012. To assess ongoing high-risk sexual behaviors after HIV diagnosis, we evaluated the proportion of HSV-2 seroconversion as well as the incidence of herpes and non-herpes STIs diagnosed during long-term follow-up.

3. Methods

All active duty USAF members diagnosed with HIV infection have mandated visits at the San Antonio Military Medical Center (SAMMC) approximately every 6 months. Screening for HSV-1 and -2 was performed at the first SAMMC visit after HIV diagnosis and periodically thereafter. All USAF members diagnosed with HIV between 1996 and 2012 with available HSV-1 and -2 serology data were included. To evaluate the change in HSV seroprevalence over time, patients were categorized into 2 groups by year of HIV diagnosis (1996–2004 and 2005–2012) similar to the recent NHANES study of HSV seroprevalence in the general US population [15]. This retrospective study was approved by the SAMMC Institutional Review Board.

HSV-1 and -2 serology for the 2 groups was evaluated at HIV diagnosis and longitudinally for those with ≥1 year of follow-up. BioPlex HSV (Bio-Rad Laboratories, Benecia, CA) is the current HSV assay and has been used in our facility since 2010. ICD-9 codes for genital herpes after HIV diagnosis were also examined to evaluate the clinical impact of HSV-1 and -2 seropositivity. As a marker for ongoing high-risk sexual behaviors, ICD-9 codes for STIs, including gonorrhea, chlamydia, and syphilis, and HSV-2 seroconversions were captured for those with ≥1 year of follow-up after HIV diagnosis. HSV serostatus and prevalence of both HSV and non-HSV STIs were compared between groups by chi-squared test and odds ratios were calculated using IBM SPSS Statistics 22.0, Chicago, Illinois.

Table 2
HSV-1 and -2 serostatus at HIV diagnosis.

Characteristic	All (*n* = 397)	1996–2004 (*n* = 131)*	2005–2012 (*n* = 266)
HSV-2 positive only	74 (18.6%)	35 (26.7%)	39 (14.7%)
HSV-1 and -2 positive	70 (17.6%)	29 (22.1%)	41 (15.4%)
HSV-1 positive only	156 (39.3%)	44 (33.6%)	112 (42.1%)
HSV-1 and -2 negative	97 (24.4%)	23 (17.6%)	74 (27.8%)

* $P < 0.01$ for HIV diagnosis between 1996 and 2004 vs. 2005–2012.

Table 3
Factors associated with HSV-2 seropositivity at HIV diagnosis.

Characteristic	Odds ratio	95% confidence interval	*P* value
Non-Caucasian race	2.19	1.33–3.60	<0.01
HIV diagnosis between 1996 and 2004	2.06	1.29–3.27	<0.01
Age >30 at HIV diagnosis	1.73	0.94–3.18	0.08
STI diagnosis prior to HIV diagnosis	1.11	0.52–2.36	0.80
Enlisted rank	0.82	0.41–1.67	0.59

STI, sexually transmitted infection.

4. Results

A total of 397 patients were evaluated, including 131 (33.0%) and 266 (67.0%) diagnosed with HIV between 1996 and 2004 and 2005–2012, respectively (Table 1). Baseline characteristics were no different between groups and the majority of patients were enlisted males with a median age of 28 years at HIV diagnosis. Patients were most commonly Caucasian (44.2%) or African American (43.4%). A total of 41 (10.3%) patients had STI diagnoses prior to HIV diagnosis. The median CD4 count (cells/uL) at HIV diagnosis was 543 (interquartile range [IQR] 399–694) and 510 (IQR 378–665) for the 1996–2004 and 2005–2012 groups, respectively ($P = 0.39$).

HSV-2 seroprevalence at HIV diagnosis decreased from the period of 1996–2004 to 2005–2012 ($P < 0.01$), while HSV-1 seroprevalence was stable (Table 2). Odds of HSV-2 seropositivity was significantly greater for non-Caucasians (odds ratio [OR] 2.19, 95% CI 1.33–3.60) and for HIV diagnosis between 1996 and 2004 (OR 2.06, 95% CI 1.29–3.27), with a trend observed for those age >30 years at HIV diagnosis (1.73, 95% CI 0.94–3.18; Table 3). A total of 81 (20.4%) patients developed STIs by ICD-9 codes after HIV diagnosis,