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Prevalence and Predictors of *Toxoplasma* Seropositivity in Women with and at Risk for Human Immunodeficiency Virus Infection

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Abstract

We assessed the prevalence and predictors of latent *Toxoplasma* infection in a large group of human immunodeficiency virus (HIV)–infected and HIV-uninfected at-risk US women. The prevalence of latent *Toxoplasma* infection was 15% (380 of 2525 persons) and did not differ by HIV infection status. HIV-infected women aged ≥50 years and those born outside of the United States were more likely to have latent *Toxoplasma* infection, with prevalences of 32% and 41%, respectively.

Toxoplasma gondii is a protozoan organism endemic worldwide and a major opportunistic pathogen in HIV-infected individuals. In HIV infection, symptomatic disease most often occurs as a result of reactivation of latent infection [1]. There is wide geographic variation in the prevalence of latent *Toxoplasma* infection. Studies from Latin America, Europe, Asia, and Africa have reported a range of prevalence estimates of 30%–75%, whereas prevalence estimates from US studies have had a range of 3%–42% [2, 3]. Although latent *Toxoplasma* infection is of great clinical importance in HIV-infected persons, there is a dearth of information concerning *Toxoplasma* seroprevalence in this population in the United States.

In the United States, seroprevalence data for HIV-infected individuals come from small, predominantly male cohorts in which the range of prevalences is 3%–22% [4, 5]. The largest US cohort, which included 403 HIV-infected men from the Multicenter AIDS Cohort Study, reported a *Toxoplasma* seroprevalence of 11% [6]. The 2 largest *Toxoplasma* seroprevalence studies of HIV-infected US women included 169 and 138 women and reported seroprevalences of 22% and 20%, respectively [7, 8]. To determine the seroprevalence of *Toxoplasma* in HIV-infected women in the United States, we tested women in the Women's Interagency HIV Study (WIHS) for antibodies to *T. gondii*.

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Methods

The WIHS is an ongoing multicenter longitudinal study of HIV-infected and at-risk HIV-uninfected women designed to examine the demographic characteristics of HIV-infected women in the United States. Enrollment occurred at 6 WIHS sites (Manhattan/Bronx, New York; Brooklyn, New York; Washington, D.C.; northern California; Los Angeles County/southern California; and Chicago, Illinois) from October 1994 through November 1995. A total of 2628 women were enrolled in the study, 2059 of whom were infected with HIV and 569 of whom were not. The rationale, recruitment information, and data collection methods have been described elsewhere [9]. In brief, study participants were recruited nonrandomly from HIV primary care clinics, hospital-based and research programs, community outreach sites, drug rehabilitation programs, support groups, and HIV testing sites, as well as via referrals from enrolled patients. At the baseline visit, women underwent an extensive interview to collect demographic and clinical information, a physical examination, and collection of blood and other specimens. In this report, we present detailed data only from the HIV-infected women, because these data are more clinically relevant, given the risk of reactivation of infection.

Appropriate written and oral informed consent was obtained from all participants in this study. Guidelines for human experimentation in accordance with the US Department of Health and Human Services and the Institutional Review Board of each participating institution were followed in the conduct of the study.

For this cross-sectional study, a case patient was defined as any woman in the WIHS with *Toxoplasma* serology documented at baseline. Serologic testing for *T. gondii* was performed by use of the Sabin Feldman dye test (J. Remington; Palo Alto, California), the standard to which other serological assays are compared [10]. A positive test result was defined as a titer of >1:16 [10].

The baseline prevalence of *Toxoplasma* infection was determined overall and stratified by the following participant characteristics: age, race/ethnicity, country of birth, employment status, income, residence status, HIV infection risk category, level of education attained, $CD4^+$ T lymphocyte count, and WIHS center of enrollment. Where reported, 95% CIs of prevalence estimates were computed assuming binomial distribution. Logistic regression methods were used to identify characteristics associated with prevalent infection. Magnitudes of associations were estimated with the OR, and corresponding 95% CI values and/or *P* values are presented. The final multiple logistic regression model was generated with use of only characteristics that had been found to be significantly associated with prevalent infection at the $\alpha = 0.05$ level on univariate analyses.

Results

A total of 2525 women (96% of WIHS participants) had *Toxoplasma* infection documented by serological testing at baseline. Among these women, 301 (15.3%) of 1973 HIV-infected (95% CI, 13.7–16.9) and 79 (14.3%) of 552 HIV-uninfected women (95% CI, 11.5–17.5) had serological test results positive for *Toxoplasma* infection. Data from the HIV-infected women are presented in detail; however, we also conducted the same analyses with use of the data for all 2525 women and found results consistent with those for the HIV-infected women (data not shown).

The prevalence of a positive serological test results (both overall and stratified by selected characteristics) among the 1973 HIV-infected women is presented in table 1. The characteristics that were significantly ($P < .05$) associated with *Toxoplasma* serostatus on univariate analysis were age, race/ethnicity, country of birth, HIV risk category, residence

status, $CD4^+$ T lymphocyte count, and WIHS site of enrollment. Income, educational attainment, and employment status were not significantly associated with serostatus. Only 3 characteristics were found to be independently associated ($P < .05$) with prevalent *Toxoplasma* infection on multiple logistic regression analyses: age, country of birth, and $CD4^+$ T lymphocyte count. Specifically, prevalent infection was higher among the following women: (1) those aged ≥50 years (OR, 3.1; $P < .0001$), compared with women aged <50 years; (2) those born outside the United States (OR, 5.4; $P < .0001$); and (3) those who had a $CD4^+$ T lymphocyte count of 200–499 cells/mm^3 (OR, 1.5; $P = .03$), compared with those who had a count of ≥500 cells/mm^3. The difference in seroprevalence for women who had a $CD4^+$ T lymphocyte count of <200 cells/mm^3 versus those who had a count of ≥500 cells/mm^3 did not reach statistical significance (OR, 1.2; $P = .3$). The 1637 US-born HIV-infected women had a seroprevalence of 10%, and only age of ≥50 years (OR, 4.1; $P < .0001$) and a baseline $CD4^+$ T lymphocyte count of <200 cells/mm^3 (compared with ≥500 cells/mm^3; OR, 1.7; $P = .03$) were significantly associated with prevalent *Toxoplasma* infection.

Discussion

To our knowledge, this is the largest study of the prevalence of latent *Toxoplasma* infection in HIV-infected individuals in the United States. Previous studies involving HIV-infected individuals have reported wide variations in seroprevalence (3%–22%) [4–8]. We found that the prevalence of positive tests for *Toxoplasma* antibody in this large cohort was 15.1%. HIV-infected women did not differ from HIV-uninfected women with regard to seroprevalence, which is consistent with the findings of previous investigators.

The largest studies to date of *Toxoplasma* seroprevalence in the US population of HIV-uninfected people or those of unknown HIV infection status are US military studies and the National Health and Nutritional Exam Survey (NHANES) study [11–13]. A large US study of 2862 military recruits conducted in 1989 [11] reported a prevalence of 9.5%, which was lower than the 14% prevalence reported in a similar study from 1965 [12]. The lower prevalence of latent *Toxoplasma* infection seen in the US military studies may be because the subjects in those studies were younger (80% were aged 17–20 years) than the subjects in ours. Also, only 9% of the military study population was Hispanic, and very few subjects were likely to be of non-US origin, although this was not specified. This prevalence of 9.5% is similar to the 10% seroprevalence noted for the 1637 US-born women in our study. The recently published study of 17,658 participants in the NHANES study from 1988–1994 found a *Toxoplasma* seroprevalence of 22.5% with an age-adjusted prevalence of 15% among women aged 15–44 years [13].

Although a number of factors, such as ethnicity and residence in New York or Los Angeles, were found to be associated with higher *Toxoplasma* seropositivity on univariate analysis, these factors were likely markers for birth outside of the United States, which was the strongest predictor of *Toxoplasma* seropositivity in this cohort, and, after age, the strongest predictor in the NHANES cohort.

We also found that women for whom injection drug use was the risk factor for HIV infection were less likely to have serological test results positive for *Toxoplasma* infection. This discrepancy may be attributable to the high *Toxoplasma* seroprevalence among women born outside the United States, who are less likely than US-born women to have acquired HIV infection through injection drug use. We are unable to explain the relationship between low $CD4^+$ T lymphocyte count and serological test results that are positive for *Toxoplasma* infection noted in this study. It is possible that women who presented with low $CD4^+$ T lymphocyte counts were more likely to be foreign born, but this association remained significant on multivariate analysis after adjusting for other variables.

Toxoplasmosis is an infection for which the prevalence in any population increases with age. Our study showed that women aged ≥50 years were more likely to be seropositive than were younger women. It could be argued that this was a cohort effect and that these women acquired disease during childhood. Women ≥50 years of age had a markedly higher seroprevalence than did women aged 40–49 years (table 1). This age-adjusted increase in prevalence was also demonstrated in the NHANES study, which recruited patients aged 1 to 170 years. These findings suggest that, in the United States, soil exposure, which occurs most frequently during childhood, may not be the principal mode of *Toxoplasma* acquisition. There were no significant differences between black and white women from the United States, which supports earlier findings that, in a given population, race does not affect seroprevalence [13].

The findings from this study should be interpreted in light of the study's limitations. Information on cat ownership, dietary habits, soil exposure, and soil-related occupations—important risk factors for disease acquisition—were not obtained during the WIHS interview. However, *Toxoplasma* seroprevalence did not vary significantly by the amount meat in the diet or cat ownership in the US NHANES cohort [13]. Another limitation was that, because this was a point prevalence study, we were unable to ascertain whether the higher prevalence associated with age of ≥50 years was a result of disease acquired during childhood or a result of continuous exposure throughout life.

Despite these limitations, we can draw the following conclusions. The prevalence of latent *Toxoplasma* infection in a large cohort of HIV-infected women and HIV-uninfected at-risk women was 15%, and the seroprevalence did not differ by HIV status. The prevalence among women born in the United States was 10% and did not differ by race when adjusted for age and $CD4^+$ T lymphocyte count. In the US population of HIV-infected women, women aged ≥50 years, women with lower $CD4^+$ T lymphocyte counts, and women born in other countries were more likely to have latent *Toxoplasma* infection.

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Table 1

Characteristics associated with *Toxoplasma* seropositivity among 1973 HIV-infected women.

Characteristic	Proportion of patients with positive results (%)[b]	Unadjusted *P* value[a]	Unadjusted OR (95% CI) (*n* = 1973)	Adjusted OR (95% CI) (*n* = 1898)
Age, years		<.0001		
<30	65/392 (16.6)		1.0	1.0
30–39	134/949 (14.1)		0.8 (0.6–1.1)	1.0 (0.7–1.4)
40–49	69/528 (13.1)		0.8 (0.5–1.1)	1.1 (0.7–1.8)
≥50	33/103 (32.0)		**2.4 (1.4–3.9)**	**3.1 (1.8–5.5)**
Race		<.0001		
White, non-Hispanic	36/363 (9.9)		1.0	1.0
Black, non-Hispanic	130/1080 (12.0)		1.2 (0.8–1.8)	1.2 (0.8–1.8)
Latina/Hispanic	123/473 (26.0)		**3.2 (2.1–4.8)**	1.5 (1–2.5)
Other	11/55 (20.0)		**2.3 (1.1–4.8)**	1.3 (0.6–3.1)
Born outside of the United States	137/333 (41.1)	<.0001	**6.3 (4.8–8.2)**	**5.5 (3.9–7.9)**
Stable housing	281/1723 (16.3)	.0006	**2.1 (1.3–3.4)**	1.5 (0.9–2.5)
HIV infection risk category		.0002		
Injection drug use	72/649 (11.1)		1.0	1.0
Heterosexual sex	131/822 (15.9)		**1.5 (1.1–2.1)**	1.1 (0.8–1.6)
Receipt of transfusion	22/80 (27.5)		**3.0 (1.8–5.3)**	1.3 (0.7–2.5)
None identified	71/403 (17.6)		**1.7 (1.2–2.4)**	1.0 (0.7–1.5)
Baseline $CD4^+$ T lymphocyte count, cells/mm^3		.051		
≥500	62/507 (12.2)		1.0	1.0
200–499	142/836 (17.0)		**1.5 (1.1–2.0)**	**1.5 (1.0–2.1)**
<200	93/576 (16.1)		**1.4 (1.0–2.0)**	1.2 (0.9–1.8)
Women's Interagency HIV Study site		.007		
San Francisco, California	31/320 (9.7)		1.0	1.0
Bronx, New York	66/409 (16.1)		**1.8 (1.1–2.8)**	1.2 (0.7–2.0)
Brooklyn, New York	52/295 (17.6)		**2.0 (1.2–3.2)**	1.2 (0.7–2.1)
Chicago, Illinois	34/259 (13.1)		1.4 (0.8–2.4)	1.5 (0.9–2.7)
Washington, D.C.	39/277 (14.1)		1.5 (0.9–2.5)	1.2 (0.7–2.1)
Los Angeles, California	79/413 (19.1)		**2.2 (1.4–3.4)**	1.1 (0.6–1.8)

NOTE. Numbers for some characteristics do not add up to 1973 because data were missing. Statistically significant results are shown in boldface.

[a] Global *P* values are based on likelihood ratio statistics.

[b] Of 1973 total patients, 15.3% were found to be seropositive for *Toxoplasma* infection.