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Seroincidence of 2009 H1N1 infection in HIV-infected and HIV-uninfected women prior to vaccine availability

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Abstract

The 2009 H1N1 pandemic was a unique opportunity to investigate differences in influenza infection using serology by HIV status. Using serial serum specimens collected from 1 April to 30 September 2009 and the prior 2 years from Women's Interagency HIV study participants, there was no difference in serologic evidence of 2009 H1N1 infection among HIV-infected women with a CD4 cell count at least 350 cells/μl compared with HIV-uninfected women. Owing to evidence showing a greater risk of influenza-related complications, HIV-infected individuals should continue to be a priority group for vaccination.

The 2009 H1N1 influenza pandemic was the first widespread outbreak of a novel influenza strain since the identification of the HIV in the early 1980s. This situation allowed for the use of serology to estimate incident infection. No large epidemiologic study has been conducted to evaluate the incidence of influenza infection in adults infected with HIV. Reports from influenza outbreaks in residential drug rehabilitation facilities conflict regarding the difference in influenza infection rates by HIV infection status [1–3]. We present data of serologic evidence of 2009 H1N1 infection in HIV-infected and similar HIV-uninfected women in the Women's Interagency HIV Study (WIHS), prior to the availability of the monovalent vaccine.

WIHS study procedures have been described elsewhere [4, 5]. Briefly, participants have semiannual study visits that include collection of blood for laboratory testing and storage in the repository. Study protocols and consent forms have been approved by institutional review boards at each study site.

Self-reports of influenza-like illnesses and assays for influenza viruses were not available; therefore, we used a hemagglutination inhibition titer at least 32 against A/California/7/09

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for serum collected from April to September 2009 as serologic evidence of infection, provided there was at least four-fold increase in titer from serum collected during April to September of 2007 or 2008 (depending upon availability of specimen in the repository). The hemagglutination inhibition assay followed standard procedures and included control sera with known titers. Participants contributed person-time from 1 April 2009 to the day sera was collected. Incidence rates per 100 person-years, adjusted incidence rate ratios (aIRR), and 95% confidence intervals (given in parenthesis) were estimated using over dispersed Poisson regression models. Data were analyzed using SAS 9.0 (SAS Institute, Inc., Cary, North Carolina, USA).

A total of 1790 (n = 1267 HIV-infected, n = 523 HIV-uninfected, median age = 45, range 25–76) women completed a study visit between 1 April and 30 September 2009 and had available serum specimens in the central repository that was used to quantify 2009 H1N1 titers (and 2008/07 titers, when necessary). The characteristics of the study population reflect the demographics of the WIHS cohort. Of these women, 121 (86 HIV-infected and 35 HIV-uninfected women) had serologic evidence of 2009 H1N1 infection. Cumulative incidence of serologic evidence of infection was 7% (121/1790) overall (HIV-infected: 7% or 86/ 1267, HIV-uninfected: 7% or 35/523).

The 1790 HIV-infected and HIV-uninfected women in our study contributed 414.74 person-years for an overall seroincidence of 29.2 (24.4–34.9) per 100 person-years; there was no difference in seroincidence by HIV status (Table 1). Among HIV-infected and HIV-uninfected women, seroincidence rates were highest among women less than 30 years of age, of non-Hispanic Black race, those with a history of injection drug use, residents of the east coast, smokers, and those with asthma. After adjustment for confounders, seroincidence was statistically significantly lower in women at least 30 years of age as compared with women less than 30 years of age. Due to the small number of HIV-infected women with a CD4 cell count less than 350 cells/μl and evidence of serologic infection (n = 15), we performed a sensitivity analysis comparing HIV-infected women with a CD4 cell count at least 350 cells/μl to HIV-uninfected women; seroincidence was similar [HIV-uninfected incidence rate = 29.7 (21.3–41.3); HIV-infected incidence rate = 33.4 (26.4–42.3); aIRR = 1.20 (0.79–1.82)].

Among HIV-infected women, those with a lower CD4 cell count (<350 cells/μl) or a clinical AIDS diagnosis had lower seroincidence rates (Table 1). After adjusting for confounders, those with an HIV-1 RNA more than 80 copies/ml had a statistically significant decrease in seroincidence. Women with a clinical AIDS diagnosis also had a decrease in seroincidence; however, the relationship was not statistically significant in multivariate analyses.

Our findings provide an understanding of influenza infection and immune responses in HIV-infected individuals, a topic that is infrequently studied. The monovalent vaccine was not available during our study period, which allowed us to attribute elevated titers to the sole cause of exposure to the novel 2009 H1N1 virus.

There was no difference in 2009 H1N1 seroincidence by HIV status when comparing HIV-infected women with a CD4 cell count at least 350 cells/μl to HIV-uninfected women in sensitivity analysis. Additional influenza testing strategies are needed to investigate incidence among HIV-infected women with a CD4 cell count less than 350 cells/μl as infections were possibly missed due to the inability to mount the adequate antibody response for our definition of infection. Among HIV-infected women, those with a detectable (>80 copies/ml) HIV-1 RNA, lower (<350 cells/μl) CD4 cell counts, and a clinical AIDS diagnosis were less likely to have serologic evidence of 2009 H1N1 infection in multivariate analyses, suggesting uncontrolled HIV infection and a lower CD4 cell count correlates with

serologic reactivity, as seen in studies of influenza vaccination response in HIV-infected adults [6–10].

Other 2009 H1N1 seroincidence studies estimated 21% of persons in Pittsburgh had become infected after the second wave of the pandemic [11]: 6% of 25–44-year-olds were infected as of September 2009 in England [12], and 6% of the general population had a 2009 H1N1 titer at least 40 as of October 2009 in Pune, India [13]. Our cumulative incidence estimate of 7% (121/1790) is similar to estimates from England and Pune. We used a person-time approach to estimate differences in seroincidence by HIV status because it reduces the misclassification that accompanies assigning our participants a serologic infection status for the entire study period (from 1 April to 30 September 2009) from titers measured in serum collected on one day within the study period. Finally, our overall seroincidence estimate of 29.4 (24.4–34.9) per 100 person-years likely overestimates the number of symptomatic infections as those with subclinical illness are included, and the generalizability of our findings may be restricted to women.

Although previous serologic studies of 2009 H1N1 have attempted to estimate cumulative incidence of infection [11–13], our study is the only one to have serological data collected via serial specimens on the same individuals, demonstrating the value of ongoing, prospective HIV studies in public health emergencies of emerging infectious diseases.

Our study is the first to estimate seroincidence of 2009 H1N1 infection in HIV-infected compared with similar HIV-uninfected adults. Although we found no difference in 2009 H1N1 infection by HIV status, continued vaccination efforts among this population are warranted due to the increased risk of severe illness and influenza-associated complications [14–18].

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Table 1

2009 H1N1 influenza infection incidence rates and adjusted incidence rate ratios (*N* = 1790), from 1 April to 30 September 2009, the Women's Interagency HIV Study.

	N	2009 H1N1 infection	Person-years[a]	IR per 100 person-years	95% CI	aIRR[b]	95% CI
Overall	1790	121	414.74	29.2	24.4–34.9	–	–
HIV-uninfected	523	35	117.99	29.7	21.3–41.3	REF	–
HIV-infected	1305	86	296.76	29.0	23.5–35.8	1.02	0.68–1.54
Age (years)							
<30	93	10	25.96	38.5	20.7–71.6	REF	–
30 to <50	140	74	271.09	27.3	21.7–34.3	0.55	0.33–0.92
≥50	549	37	117.70	31.4	22.8–43.4	0.55	0.32–0.96
Race							
Non-Hispanic Black	1053	72	220.47	32.7	25.9–41.1	REF	–
Hispanic	511	34	121.77	27.9	20.0–39.1	0.80	0.52–1.22
Other	267	15	72.50	20.7	12.5–34.3	0.68	0.39–1.22
HIV transmission risk							
Injection drug use	332	27	70.77	38.2	26.2–55.6	REF	–
Heterosexual contact	696	43	162.94	26.4	19.6–35.6	0.61	0.39–0.95
Transfusion	33	2	5.68	35.2	8.8–140.9	0.85	0.20–3.57
Other	757	49	175.36	27.9	21.1–37.0	0.58	0.38–0.89
Center							
New York	755	54	159.55	33.8	25.9–44.2	REF	–
Washington DC	252	18	53.03	33.9	21.4–53.9	1.02	0.60–1.74
Los Angeles	336	23	92.12	25.0	16.6–37.6	0.77	0.46–1.28
San Francisco	231	12	54.44	22.0	12.5–38.8	0.58	0.30–1.10
Chicago	232	14	55.60	25.2	14.9–42.5	0.69	0.38–1.23
Not a smoker	1041	72	254.57	28.3	22.4–35.6	REF	–
Smoker	717	48	150.73	31.8	24.0–42.3	0.97	0.67–1.41
No asthma	1217	80	288.62	27.7	22.3–34.5	REF	–
Asthma	570	41	125.36	32.7	24.1–44.4	1.13	0.77–1.66
HIV-infected women (*N* = 1 267)							

	N	2009 H1N1 infection	Person-years[a]	IR per 100 person-years	95% CI	aIRR[b]	95% CI
CD4 T-lymphocyte count[c] (cells/μl)							
<200	159	6	39.04	15.4	6.9–34.2	REF	–
200 to <350	207	9	50.05	18.0	9.4–34.6	0.89	0.35–2.22
350 to <500	256	22	57.27	38.4	25.3–58.3	1.58	0.73–3.38
≥500	620	49	142.10	34.5	26.0–45.6	1.31	0.64–2.69
HIV-1 RNA[c] (copies/ml)							
≤80	726	63	171.45	36.7	28.7–47.0	REF	–
>80	499	23	114.46	20.1	13.4–30.2	0.55	0.33–0.92
Clinical AIDS diagnosis[d]							
No	734	55	176.30	31.2	24.0–40.6	REF	–
Yes	533	31	120.46	25.7	18.1–36.6	0.78	0.49–1.25

aIRR, adjusted rate ratio; CI, confidence interval; IR, incidence rate.

[a] Person-years were calculated from 1 April 2009 to the time the serum specimen was collected.

[b] Among HIV-infected and HIV-uninfected women: adjusted for age, race and ethnicity, HIV transmission risk, center, smoking, and asthma. Among HIV-infected women: adjusted for age, race and ethnicity, HIV transmission risk, center, smoking, asthma, CD4 cell count, HIV-1 RNA, clinical AIDS diagnosis, and self-reported highly active antiretroviral therapy use.

[c] Measured from 1 April 2008 to 31 March 2009.

[d] Clinical AIDS was classified as a prior self-report of a clinical diagnosis defined by the 1993 Centers for Disease Control and Prevention surveillance definition, excluding CD4 cell count less than 200 cells/μl (Centers for Disease Control and Prevention, 1992); measured as of 1 April 2009.