Short Communication

Lack of Occult HIV Infection Among Non-AIDS-Defining Cancer Patients in Three Academic Oncology Clinics in the United States

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Abstract

The Centers for Disease Control (CDC) testing recommendations suggest universal opt-out testing in all health care settings, including cancer clinics. The incidence of non-AIDS-defining cancers (NADCs) is on the rise among HIV patients. However, to date, no data exist on the prevalence of HIV infection among NADC patients in the United States. Knowledge of HIV infection may affect clinical management, prognosis, and overall patient survival and decrease new infections in the population. The purpose of this study was to determine the point seroprevalence of HIV infection in cancer patients being seen in medical oncology clinics. A total of 634 individuals (mean age=53.2 years) participated and were tested for HIV. None of the participants tested positive for HIV in any of the three clinics. Using a futility analysis, the upper end of the 95% confidence interval for prevalence of undiagnosed HIV in cancer patients was less than 0.3%. Most participants were female (59.2%) and non-Hispanic (96.6%). The majority of study participants were white (76.5%) or African-American (17.7%). Breast cancer (19.7%), colon cancer (10.3%), and melanoma (9.7%) were the most commonly reported non-AIDS-defining cancers. While our study suggested that there was no occurrence of undiagnosed HIV among NADC patients, it is important to note that our population was largely white, females with insurance and with a different distribution of cancer than the most prevalent NADC among HIV patients. Furthermore, one-third of the patients did not consent to participate and further studies are needed to assess reasons for their unwillingness along with other populations, specifically minorities and individuals with low socioeconomic status (SES).

HUMAN IMMUNODEFICIENCY virus (HIV) and acquired immunodeficiency syndrome (AIDS) remain leading causes of illness and death in the United States. Since the first case reported in 1981, the Centers for Disease Control and Prevention (CDC) has estimated that more than 1.7 million people in the United States have been infected with HIV including over 600,000 who have died and approximately 1.2 million who are currently living with HIV.¹ It is estimated that, 20% (about 220,000) of HIV-infected individuals are unaware of their infection and about 32% are diagnosed late when the disease has progressed.¹ Despite much effort to reduce new infections, the annual incidence of HIV has been stable in the past few years, with between 45,000 and 53,200 new cases between 2007 and 2010 (47,500 in 2010) in the United States.² This estimate is based on prevalence estimates primarily among high-risk individuals identified

from active surveillance among various populations in the United States. It is of great public health importance, and yet remains a substantial challenge, to identify individuals with undiagnosed HIV and link them to clinical care, which will improve their health outcomes and limit further transmission. Individuals unaware of their HIV infection, including cancer patients and specifically those with non-AIDS-defining cancers (NADCs), are unable to take advantage of life-saving HIV treatments, and may unknowingly infect others. In 2006, the CDC revised its recommendations for HIV testing in healthcare settings to include opt-out HIV testing as a routine part of medical care for all patients, ages 13–64, without the necessity for separate written consent or for pretest HIV counseling.³ However, despite the CDC's recommendations, very few providers have incorporated routine HIV testing into their practice.

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TABLE 1. CHARACTERISTICS OF SCREENED CANCER PATIENTS ATTENDING ONCOLOGY CLINICS AT BIRMINGHAM, ALABAMA, CHAPEL HILL, NORTH CAROLINA, AND SAN DIEGO, CALIFORNIA

	All (n = 668)	95% CI	Birmingham (n = 308)	95% CI	Chapel Hill (n = 326)	95% CI	San Diego (n = 34)	95% CI
Age (mean)	53.2 ± 10.5	(51.9–56.6)	57.9 ± 15.1	(56.3–59.6)	47.6 ± 9.7	(46.6, 48.7)	58.9 (9.6)	(55.6–62.3)
Gender								
Male	272 (40.7)	(37.1–44.4)	149 (48.4)	(42.8–53.9)	100 (30.7)	(25.9–35.9)	23 (69.7)	(50.9–80.9)
Female	395 (59.2)	(55.4–62.8)	159 (51.6)	(46.04–57.2)	226 (69.3)	(64.3–74.2)	10 (30.3)	(16.8–46.2)
Ethnicity								
Hispanic/Latino	23 (3.4)	(2.3–5.1)	4 (1.31)	(0.03–2.57)	9 (2.8)	(1.5–5.2)	10 (29.4)	(16.8–46.2)
Non-Hispanic	642 (96.6)	(94.4–97.3)	301 (98.37)	(96.07–99.39)	317 (97.2)	(94.8–98.5)	24 (70.6)	(53.8–83.2)
Race								
Black	118 (17.7)	(15.0–20.7)	54 (17.7)	(13.3–21.8)	64 (19.6)	(15.7–24.3)	0 (0)	0 (0)
White	511 (76.5)	(73.1–79.6)	243 (79.4)	(74.3–83.5)	241 (73.9)	(68.7–78.5)	27 (84.4)	(63.2–89.7)
American Indian	8 (1.2)	(0.6–2.4)	1 (0.3)	(0.0–0.9)	6 (1.8)	(0.8–4.2)	1 (3.1)	(0.5–14.9)
Asian	10 (1.5)	(0.8–2.7)	1 (0.3)	(0.0–0.9)	6 (1.8)	(0.8–4.2)	3 (9.4)	(3.0–22.9)
Other	13 (2)	(0.3–2.4)	6 (1.9)	(0.0–3.1)	6 (1.8)	(0.4–3.1)	1 (3.1)	(0.5–14.9)
Insurance								
Yes	613 (93.5)	(89.4–93.6)	292 (98.3)	(96.4–99.6)	288 (88.3)	(84.2–91.5)	33 (100.0)	(90.0–100.0)
No	43 (6.5)	(4.8–8.6)	5 (1.7)	(0.21–3.03)	38 (11.7)	(8.6–15.6)	0 (0)	0 (0)
Primary insurance								
Private HMO	41 (6.2)	(4.6–8.2)	19 (6.5)	(3.5–8.9)	18 (5.5)	(3.5–8.6)	4 (12.1)	(4.7–26.6)
Private insurance	365 (54.7)	(50.8–58.4)	142 (48.8)	(40.5–51.7)	209 (64.1)	(58.8–69.1)	14 (42.4)	(26.4–57.8)
Medicaid	50 (7.5)	(5.7–9.7)	11 (3.8)	(1.5–5.6)	31 (9.5)	(6.8–13.2)	8 (24.2)	(12.4–40.0)
Medicare	134 (20.1)	(17.2–23.3)	106 (36.4)	(29.1–39.7)	25 (7.7)	(5.3–11.1)	3 (9.1)	(3.0–22.9)
Other	22 (3.4)	(1.1–4.2)	13 (4.5)	(1.9–6.5)	5 (1.5)	(0.1–2.9)	4 (12.1)	(4.7–26.6)
Smoking status								
Never	487 (74.0)	(69.4–76.1)	185 (61.8)	(54.6–65.5)	275 (84.4)	(80.0–87.9)	27 (81.8)	(63.2–89.6)
Some days	40 (6.1)	(4.4–8.1)	18 (6.02)	(3.2–8.5)	18 (5.5)	(3.5–8.6)	4 (12.1)	(4.7–26.6)
Every day	57 (8.7)	(6.6–10.9)	23 (7.7)	(4.5–10.4)	32 (9.8)	(6.9–13.7)	2 (6.1)	(1.6–19.1)
Former	74 (11.2)	(8.9–13.7)	73 (24.4)	(18.9–28.5)	1 (0.3)	(0.02–1.9)	0 (0)	0 (0)
Drink alcohol								
Never	396 (60.0)	(55.5–62.9)	189 (63.4)	(55.9–66.8)	190 (58.3)	(52.9–63.5)	17 (53.1)	(34.1–65.9)
Some days	242 (36.9)	(32.7–40.0)	101 (33.9)	(27.5–38.0)	127 (39.0)	(33.8–44.4)	14 (43.8)	(26.4–57.8)
Every day	18 (3.1)	(1.7–4.2)	8 (2.7)	(0.8–4.4)	9 (3.7)	(1.5–5.2)	1 (3.1)	(0.5–14.9)

(continued)

TABLE 1. (CONTINUED)

	All (n=668)	95% CI	Birmingham (n=308)	95% CI	Chapel Hill (n=326)	95% CI	San Diego (n=34)	95% CI
Previous HIV test								
Yes	281 (42.1)	(38.4-45.9)	95 (30.8)	(25.7-36.0)	170 (52.2)	(46.7-57.5)	16 (47.1)	(31.5-63.3)
No	343 (51.3)	(47.6-55.1)	191 (62.0)	(56.6-67.4)	138 (42.3)	(37.1-47.8)	14 (41.2)	(26.4-57.8)
Unknown	44 (6.6)	(5.0-8.7)	22 (7.1)	(4.3-10.0)	18 (5.5)	(3.5-8.6)	4 (11.8)	(4.7-26.6)
Cancer diagnosis								
Yes	609 (91.2)	(88.8-93.1)	258 (83.8)	(79.6-87.9)	318 (97.6)	(95.2-98.7)	33 (97.0)	(83.0-99.4)
No/newly referred	59 (8.8)	(5.2-9.1)	50 (16.2)	(8.7-18.3)	8 (2.4)	(1.1-4.4)	1 (3.0)	(0.5-14.9)
Cancer type								
Breast	126 (19.7)	(16.1-22.0)	42 (15.1)	(11.3-19.7)	84 (25.8)	(21.3-30.8)	0 (0)	0 (0)
Colon	66 (10.3)	(7.8-12.4)	12 (4.3)	(2.5-7.4)	38 (11.7)	(8.6-15.6)	16 (48.4)	(31.1-66.2)
Esophagus	25 (3.9)	(2.6-5.5)	12 (4.3)	(2.5-7.4)	11 (3.4)	(1.9-5.9)	2 (6.1)	(1.7-19.6)
Lung	44 (6.9)	(4.9-8.7)	29 (10.4)	(7.3-14.5)	15 (4.6)	(2.8-7.5)	0 (0)	0 (0)
Lymphoma	51 (8.0)	(5.9-9.9)	41 (14.7)	(11.0-19.3)	10 (3.1)	(1.7-5.6)	0 (0)	0 (0)
Melanoma	62 (9.7)	(7.3-11.7)	2 (0.7)	(0.2-2.6)	60 (18.4)	(14.6-22.9)	0 (0)	0 (0)
Rectal	28 (4.4)	(2.9-6.0)	17 (6.2)	(3.8-9.5)	11 (3.4)	(1.9-5.9)	0 (0)	0 (0)
Thyroid	15 (2.4)	(1.4-3.7)	3 (1.1)	(0.3-3.1)	12 (3.7)	(2.1-6.3)	0 (0)	0 (0)
Kidney	17 (2.7)	(1.6-4.0)	17 (6.1)	(3.8-9.5)	0 (0)	0 (0)	0 (0)	0 (0)
Leukemia	15 (2.4)	(1.4-3.7)	15 (5.4)	(3.3-8.7)	0 (0)	0 (0)	0 (0)	0 (0)
Other	189 (29.6)	(25.0-31.8)	89 (31.9)	(26.5-37.8)	85 (26.1)	(21.6-31.1)	15 (45.5)	(29.8-62.0)

Following the advent of effective antiretroviral therapy (ART), medical treatment for HIV has been continuously improving and the average life expectancy has dramatically improved for HIV patients in the United States.⁴ The increased lifespan of HIV patients has created a rise in the frequency of chronic illnesses including cancer, which was not seen during the pre-ART era.⁵ The ability to track the epidemic of HIV and cancer is important as cancer is emerging as an important cause of deaths in HIV. HIV status clearly impacts the prognosis for cancer and overall survival; thus, identifying those with cancer who are HIV infected is important so that therapy may be effectively initiated, cancer treatment side effects and toxicities better anticipated, and outcomes better predicted. Most often AIDS-defining cancers are used as indicators for targeted HIV screening. Yet it remains unknown how many NADC patients attending oncology clinics may have undiagnosed (occult) HIV infection. The goal of our study was to estimate the point prevalence of HIV infection in NADC patients as a potential source of occult HIV infections. To date, no data exist on the prevalence of HIV infection among NADC patients in the United States. In a pilot study conducted among lymphoid cancer patients in a tertiary center in Nigeria, 4% of the patients were HIV positive.⁶ While Kaposi sarcoma, non-Hodgkin lymphoma, and cervical cancer are considered AIDS-defining cancers, HIV-positive individuals are also more likely than the general population to develop Hodgkin lymphoma, liver cancer, anal cancer, and stomach cancer, all known to have infectious causes.^{7–10} While most cancers associated with HIV are associated with an oncogenic viral infection, there is an increasing amount of literature suggesting a higher incidence of non-viral-related cancers in HIV-positive individuals than in the general population.¹¹ Previous reports from the AIDS-Cancer Registry Match study have shown the incidence of lung cancer to be higher in individuals with AIDS than it is for the general population.¹²

We conducted a study to test patients for HIV in three oncology clinics [University of Alabama at Birmingham (UAB), University of North Carolina (UNC)–Chapel Hill, and University of California, San Diego (UCSD)] within NCI-supported comprehensive cancer centers located at CFAR Network of Integrated Clinical Systems (CNICS) institutions. All participating individuals were required to sign informed consent forms. Study protocols were approved by the Institutional Review Board at all three universities. The patients visiting the cancer clinic were counseled before the test about HIV with arrangements to be referred to the HIV clinic if they were positive. Following the standard protocol, an OraQuick rapid HIV test (sensitivity 99.3%, specificity 99.98%) was performed using a noninvasive mouth swab. The test was completed while the patients waited to meet their physician and results were delivered prior to their leaving. An individual's type of cancer was self-reported and confirmed from the medical chart. Some of the patients were newly referred and did not have a confirmed diagnosis of cancer. Demographic information and other relevant clinical information were obtained on all tested individuals.

A total of 987 patients were approached to participate in the study (517 at UAB, 436 at UNC, and 34 at UCSD); of these 634 (66.5%) consented: 308 (59.6%) at UAB, 326 (74.8%) at UNC, and 34 at UCSD (Table 1). The mean age of the overall participants was 53.2 years, with relatively older individuals in Birmingham and younger individuals in Chapel Hill. Most

participants were female (59.2%) and non-Hispanic (96.6%). The majority of study participants were white (76.5%) or African-American (17.7%). Most participants did not currently smoke (74%) or drink alcohol (60%). Of those patients who consented to participate, most (51.3%) had never been tested for HIV. Breast cancer (19.7%), colon cancer (10.3%), and melanoma (9.7%) were the most common self-reported malignancies among these patients (Table 1). About one-third of study participants reported a type of cancer, which by itself was not frequent (<2%). The majority of patients paid for medical care through private insurance (60.9%) or Medicare (20.1%), with less than 10% of patients using Medicaid or paying out of pocket for health services. None of the participants tested positive for HIV in any of the three clinics. Using a futility analysis, the upper end of the 95% confidence interval for prevalence of undiagnosed HIV in cancer patients was less than 0.3% in this population in the three urban clinical setting.

Cancers associated with immunosuppression from increased age could mask an underlying HIV infection that could go unnoticed by health care professionals. For example, the risk for developing lung cancer increases with age and with HIV infection.⁵ Older individuals with lung cancer who do not overtly fit the risk profile of patients with HIV could have HIV infection overlooked in management of their cancer. Given potential differences in the prognosis and management of cancers presenting with HIV, missing a coexisting HIV infection could impair optimal clinical management. The ability to track the epidemic of HIV and cancer, specifically NADC, is important since there are potential differences in prognosis and management of cancers presenting with HIV. In 34 U.S. states that reported AIDS during 2004–2007, an estimated number of AIDS-defining cancer was 7,869 and NADC was 7,563.¹³ Overall, reports of NADC has increased steadily from 1991 to 2005 and has exceeded the annual number of AIDS-defining cancers since 2003. In the United States, lung cancer, anal cancer, liver cancer, and Hodgkin lymphoma are the most prevalent NADCs among HIV patients.¹³ However, in our study, breast cancer, colon cancer, esophageal cancer, and lung cancer were the four most prevalent cancers. Based on the national survey of 34 states in the United States during 2004–2007, these cancers comprised only 7.5%, 6.2%, 1.1%, and 20.7%, respectively, of the 2191 NADC reported.¹³ Thus, the oversampling of patients with these cancers (low prevalence other than lung cancer) in our population might explain why we did not observe any HIV-positive patients. Following the IRB guidelines, we were not able to determine the distribution of the cancer type among those who did not consent to participate in the study.

The prevalence of HIV infection in the general adult population in the United States is estimated to be 0.45% and as high as 2.1% among heterosexuals living in high-poverty urban areas.¹⁴ Although we had enough power to detect a few undiagnosed HIV⁺ individuals among our sample size of 634 in the three sites, caution is required in interpreting and generalizing the results. Our population was composed largely of white, female, and insured individuals, whereas the epidemic of HIV seems more prevalent among black, male, and uninsured individuals. As described above, the patient pool of cancer type is different than the prevalent NADC observed among HIV patients. Of note, one-third of the patients did not consent to participate, so their cancer type could

not be known. In one study using the discarded blood samples in an urban emergency department, it was found that the prevalence of undiagnosed HIV was higher in individuals who declined HIV screening versus those who consented (3% vs. 0.7%).¹⁵ Thus, further studies are required to assess the reasons for patients who opt out of HIV testing.

Some of the patients approached did not believe that they were at risk for HIV; others were too sick and had several clinical tests to be performed and did not have time, interest, or energy for additional tests. Most cancer patients are accompanied to the clinic and it is possible that they may not feel comfortable being tested for HIV because of the stigma associated with having to reveal their risky behaviors to their partner. Revealing their HIV status to their primary partner might be a significant barrier preventing individuals from enrolling in our study. Male self-disclosure of HIV-positive serostatus to a primary sex partner ranges from 67 to 88%, suggesting that over 25% of individuals with HIV-positive partners do not know that they are at risk of contracting HIV.¹⁶ Other studies have reported that 17–32% of both men and women fail to disclose their serostatus to their partners.¹⁷ The FDA recently approved a take home OraQuick test, and perhaps this may provide an option for everyone to be tested in private and seek medical care. However, it is important to educate everyone of the availability of this test to achieve the goal.

Our study population is composed of individuals with high socioeconomic status (SES), as evident from the large proportion of people with private insurance or Medicare coverage (81.0%), and might not represent the population with occult HIV in the United States. Low SES is associated with less access to health care, lower levels of education, and increased risk of contracting HIV. While our study suggested that there was no occurrence of occult HIV among NADC patients, further studies are needed to assess the reasons for the unwillingness of one-third of these patients to participate and also how the prevalence could vary in other populations, specifically minorities and individuals with low SES. Providers need to increase HIV testing with their cancer patients, especially since many will undergo immunosuppressive chemotherapy and radiotherapy.

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