Prevalence and Correlates of Unknown HIV Infection Among Patients Seeking Care in a Public Hospital Emergency Department

NICOLA M. ZETOLA, MD, MPH^a Beth Kaplan, MD^b Teri Dowling, MPH, MA^c Trevor Jensen, BS^d Brian Louie, BA^c Mahtab Shahkarami, BS^c Grant Colfax, MD^c Jeffrey D. Klausner, MD, MPH^{a,c,d}

SYNOPSIS

Objectives. Screening for human immunodeficiency virus (HIV) infection in the emergency department (ED) has been proposed as an effective approach to increase early HIV diagnosis. To evaluate the potential for the implementation of routine screening, we determined the prevalence of unknown HIV infection among patients being seen in an urban public hospital ED.

Methods. We conducted a cross-sectional study among patients presenting to the San Francisco General Hospital's ED during March 2007. We reviewed patients' medical records to determine HIV infection status. In patients with unknown or negative HIV-infection status, we tested de-identified remnant blood specimens by HIV-antibody and nucleic-acid assays. We used a sensitive/ less sensitive testing algorithm to determine the duration of HIV infection.

Results. During the study period, 1,820 patients had blood collected for clinical evaluation. Of those patients, 146 (8.0%) were known to be HIV-infected. Among the remaining 1,674 patients with unknown HIV-infection status, HIV-infection prevalence was 0.9% (15 of 1,674, 95% confidence interval [CI] 0.55, 1.47). In addition, one case of acute HIV infection (HIV-antibody negative, HIV RNA detected) was identified. Patients with unknown HIV infection vs. those who were uninfected were more likely to be homeless (odds ratio [OR] = 3.89, 95% CI 1.32, 11.45, p<0.05) and 18 to 30 years of age (OR=3.15, 95% CI 1.03, 9.61, p<0.05).

Conclusions. In a sample of patients visiting a county ED, the relative prevalence of unknown HIV infection (10%) was modest and less than national estimates (25%). Acutely HIV-infected patients might account for a significant proportion of those with unknown HIV infection in an ED setting.

^aDivision of Infectious Diseases, Department of Medicine, University of California, San Francisco, CA

^bDepartment of Emergency Medicine, University of California, San Francisco, CA

^cSan Francisco Department of Public Health, San Francisco, CA

^dSchool of Medicine, University of California, San Francisco, CA

Address correspondence to: Jeffrey D. Klausner, MD, MPH, STD Prevention and Control Services, San Francisco Department of Public Health, 1360 Mission St., Ste. #401, San Francisco, CA 94103; tel. 415-355-2000; fax 415-554-9636; e-mail <Jeff.Klausner@sfdph.org>. ©2008 Association of Schools of Public Health

Approximately one-fourth of the one million to 1.2 million people infected with human immunodeficiency virus (HIV) in the United States may be unaware of their infection.^{1,2} Those people are missing the opportunity to receive lifesaving antiretroviral therapy and take preventive measures to reduce HIV transmission. Some studies have estimated that HIV transmission from people unaware of their infection accounts for about half of the new HIV infections each year.^{1,3,4} In addition, many newly identified HIV-infected people are diagnosed late in the course of disease.⁵⁻⁹ Several studies have found that these late testers (particularly those from certain minority groups) and patients unaware of their HIV infection make multiple contacts with health-care systems during the years prior to diagnosis.¹⁰⁻¹³ In particular, the emergency department (ED) often serves as the primary source for medical care for these populations.^{11,14,15} HIV screening in the ED and other health-care settings has proved to be feasible.16-19

Knowledge of the prevalence and characteristics of patients with unknown HIV infection is critical for informing the development of screening guidelines and approaches in ED settings. Studies performed in the U.S. suggest that the prevalence of HIV infection among patients seeking care in the ED ranges from 2% to 17%, with a prevalence of unknown HIV infection ranging from 1% to 5%.16,20 However, most of those studies are outdated. Acute HIV infection refers to the highly infectious period, typically one to six weeks in HIV-infected patients, between exposure to HIV and the development of detectable antibodies against HIV. During that period, approximately half of HIV-infected patients develop a variety of symptoms that, in many cases, precipitate encounters with an ED.²¹ Although some experts believe that acute HIV screening should be implemented in EDs and urgent care settings, very few studies have looked into the prevalence of acute HIV infection in EDs in the U.S.^{22–24}

To determine the best HIV screening strategy in any given population, an accurate description of the prevalence and characteristics of individuals with unknown HIV infection in such a population is highly desirable.¹⁸ A limited number of studies have looked directly into the prevalence and risk factors of HIVinfected patients seeking care in EDs who are unaware of their infection.^{18,19,25} To evaluate the potential for the implementation of routine screening, we determined the prevalence of unknown HIV infection among patients being seen in our urban public hospital ED.

METHODS

Study design

We conducted a cross-sectional, unlinked HIV seroprevalence survey among patients with unknown or negative HIV serostatus who had blood drawn for routine medical care at the San Francisco General Hospital (SFGH) ED during March 2007.

Population and procedures

The survey included all patients seeking medical attention at the SFGH ED during the study period who had blood specimens collected as a part of their routine medical care. The SFGH ED receives approximately 50,000 patient visits per year, predominantly from individuals who are uninsured (30%) or receiving public insurance (40%). It is the only level I trauma center in San Francisco City and County (population 780,000). We determined the HIV status of patients by reviewing medical records dated from January 1996 through March 2007. We categorized patients as HIV-infected if medical records included (1) a positive HIV enzyme immunoassay (EIA) test; (2) a positive HIV Western blot test; (3) a positive HIV RNA test; (4) mention of any HIV diagnosis and/or acquired immunodeficiency syndrome (AIDS)-defining opportunistic infection by International Classification of Diseases, 9th and 10th Revisions (ICD-9 and ICD-10) coding; (5) HIV-related medical care visit at the SFGH Medical Center; or (6) any prescription for highly active antiretroviral therapy.

In patients without any documentation of HIV infection, we de-identified patient whole-blood specimens and tested those for HIV infection by HIV antibody. Negative HIV-antibody specimens were further tested for the presence of HIV RNA. We reviewed hospital and laboratory databases up to three months after the last patient visit to determine any new HIV diagnosis after the ED encounter. The number of visits to the ED, urgent care clinic, and other health-care settings associated with the SFGH Medical Center during the 30 days before and the 30 days after the ED encounter were measured. Only clinical encounters recorded in The Health Records Electronic Data Set (THREDS, described later in this article) were used in this study.

Given that no standard definition for frequent visitors to the ED is available, patients with more than one ED encounter during the study period (30 days) were considered patients with frequent visits to the ED and were compared with patients with only one ED encounter. For all patients, we analyzed encounters with the health-care system during the 30 days before the first ED encounter and the 30 days after the last ED encounter. Unclassified patients were defined as patients for whom some basic information (first and last name) was lacking during the ED encounter. These patients were a heterogeneous group of people consisting usually of unconscious patients, trauma victims, and/or other patients with an impaired level of consciousness, as well as those with lack of documentation that prevented their identification on triage.

Five different databases were sequentially generated to ensure that no linkage of HIV test results to identifying patient information was possible. First, a database with the patient's demographic characteristics, medical chart information, and SFGH clinical laboratory results was created. This database did not include the unique study identification number. Second, a temporary linkage database consisting of SFGH medical record numbers and the unique study identification number was created. Third, a database was created containing the unique study identification number linked to the patient demographic and clinical data. This database contained no personal identifiers. Fourth, the San Francisco Department of Public Health (SFDPH) Laboratory tested blood specimens identified only by the unique study identification number. After we confirmed that all patient information was accurate and complete, the first two databases (the only ones containing any personal identifiers and/or allowing linkage to personal identifiers) were permanently destroyed and HIV testing was started. Finally, we created a fifth database by merging the database with the study identification number and patient characteristics with the SFDPH Laboratory database containing the results of the HIV testing for analysis.

Data source

We obtained all patient information from THREDS from the University of California, San Francisco (UCSF) Clinical and Translational Science Institute (CTSI) Clinical Research Center at SFGH and from manual review of the individual hospital medical records.

Laboratory testing

Patient plasma samples were screened for HIV antibodies by EIA (Genetic Systems[™] HIV-1/HIV-2 Plus O EIA, Bio-Rad Laboratories, Hercules, California). Reactive EIA samples were tested for confirmation using an immunofluorescent assay (IFA) (Fluorognost HIV-1 IFA, Sanochemia Pharmazeutika AG, Vienna, Austria). Samples with discordant EIA and IFA results were further evaluated by testing for HIV-1 RNA using Transcription Mediated Amplification (TMA, Aptima HIV-1 RNA Qualitative Assay, Gen-Probe Inc., San Diego, California). Patients with reactive EIA samples that tested IFA and TMA negative were considered not infected with HIV. All confirmed positive samples were tested by an EIA modified to be less sensitive (Vironostika-LS HIV-1 Microelisa, BioMérieux Inc., Durham, North Carolina) as utilized in the Serologic Testing Algorithm for Determining Recent HIV Seroconversion (STARHS) method to look for evidence suggestive of recent infection.^{26,27} All testing was performed at the SFDPH Laboratory. HIV antibody-negative specimens were tested with a pooled RNA screening protocol by Abbott real-time polymerase chain reaction (PCR) assay (Abbott Laboratories, Abbott Park, Illinois).

Outcomes

The primary outcome of our study was the prevalence of unknown HIV infection. Potential correlates of unknown infection included age, sex, race/ethnicity, health insurance status, marital status, primary language, previous HIV testing, frequency of visits to the ED and urgent care clinic during the prior 30 days, homelessness status, and admission to the hospital.

Statistical analyses

Given that a patient could have multiple visits to the ED without increasing the number of patients with unknown HIV infection during the study period, all analyses were performed at the patient level (as opposed to the visit level). The prevalence of unknown HIV infection and 95% confidence intervals (CIs) were determined by standard methods. Odds ratios were calculated for all factors potentially associated with unknown HIV infection. We controlled for possible confounding or effect-modifying factors by creating a logistic regression model using backward stepwise elimination. We determined variables included in the logistic regression analysis a priori based on estimation of their significance as epidemiologic factors during the preliminary crude analysis (significant at $p \le 0.05$) and biological plausibility. The model included all of the following variables: age, sex, health insurance status, race/ethnicity, previous HIV testing, marital status, frequency of visits to the ED and urgent care clinic during the prior 30 days, homelessness status, primary language, and admission to the hospital. A two-sided p-value < 0.05 was considered statistically significant, and we used SAS version 9.1 for analyses.²⁸

Human subjects

The UCSF Committee on Human Research approved this study and waived patient consent requirements.

RESULTS

During the study period (March 2007), 1,820 out of 3,673 patients had blood specimens collected at the SFGH ED. Of those 1,820 patients, we determined 146 (8.0%) to be HIV-infected by medical record review. Table 1 shows the characteristics of patients seeking care at the SFGH ED by calendar year 2006, overall for March 2007, and our study sample from March 2007.

Of the 1,674 patient specimens tested among patients not known to be HIV-infected, 15 patients (0.9%, 95% CI 0.55, 1.47) were found to be HIV-infected (Table 2). The characteristics of these 15 patients are shown in Table 3. One HIV RNA-positive specimen (6.7% of those with unknown HIV infection, 95% CI 1.55, 30.23) was detected among the HIV-1

antibody-negative specimens. Interestingly, seven of the 15 patients (47.0%) with unknown HIV infection had at least one other visit to the ED or the urgent care clinic during the previous month. Furthermore, three (20.0%) were admitted to the hospital and discharged without an HIV diagnosis. None of the unknown HIV-infected patients had evidence of recent infection by detuned EIA and, therefore, were likely to have chronic (not recent) HIV infection.

The odds ratios for selected factors associated with unknown HIV infection are shown in Table 4. Being male and homeless were significantly associated with unknown HIV infection (Table 4). In the multivariate analysis, being homeless and aged 18 to 30 years were found to be statistically associated with unknown HIV infection (Table 4).

Table 1. Characteristics of San Francisco General Hospital emergency department patients during 2006, March 2007, and included in March 2007 study of unknown HIV infection prevalence

	2006ª Number (percent)	March 2007 ^ь Number (percent)	Study sample ^c Number (percent)
Gender Male Female	30,749 (62.4) 18,535 (37.7)	2,226 (62.3) 1,348 (37.7)	1,043 (62.3) 631 (37.7)
Age (in years) 18–30 31–45 >45	11,750 (23.7) 14,922 (30.1) 20,285 (40.9)	850 (24.9) 995 (29.1) 1,507 (44.1)	290 (17.7) 413 (25.2) 937 (57.1)
Language English Spanish Other Unknown	32,882 (65.5) 4,614 (9.2) 3,383 (7.1) 9,094 (18.1)	1,984 (54.0) 263 (7.1) 268 (7.3) 1,158 (31.0)	1,255 (75.0) 209 (12.5) 117 (7.0) 93 (5.6)
Insurance Uninsured Public Private	25,454 (51.5) 19,492 (39.5) 2,137 (4.3)	1,809 (50.1) 1,394 (38.6) 142 (3.9)	804 (48.1) 768 (45.9) 102 (6.0)
Race/ethnicity White Black Latino Other Unknown	14,479 (28.9) 14,565 (29.0) 11,593 (23.1) 7,923 (15.8) 1,613 (3.2)	1,007 (27.4) 1,042 (28.4) 829 (22.6) 647 (17.6) 148 (4.0)	423 (25.3) 477 (28.5) 387 (23.1) 306 (18.2) 81 (4.9)
Homeless	8,299 (16.5)	600 (16.3)	304 (18.3)
Unclassified ^d	2,689 (5.4)	62 (1.8)	34 (2.0)
Admitted to the hospital	9,523 (19.0)	872 (23.7)	844 (50.8)
Total	50,173 (100.0)	3,673 (100.0)	1,674 (100.0)

^aIncludes all visits for the calendar year 2006. Multiple visits for individual patients are possible.

^bIncludes the number of individual (de-duplicated) patients seen at the emergency department from March 1 to March 31, 2007.

Includes the number of individual (de-duplicated) patients included in the study sample from March 1 to March 31, 2007.

^dUnclassified refers to patients for whom some basic information (first and last names) was lacking during the emergency department encounter. HIV = human immunodeficiency virus

	Study sample Number (percent)	Number of patients with unknown HIV infection (n=15)	Prevalence (percent) per 100 patients (95% confidence interval)
Gender Male Female	1,043 (62.3) 631 (37.7)	13 2	1.2 (0.67, 2.12) 0.3 (0.01, 1.01)
Age (in years) ^a 18–30 31–45 >45	290 (17.7) 413 (25.2) 937 (57.1)	5 2 7	1.7 (0.56, 3.98) 0.5 (0.06, 1.74) 0.7 (0.37, 1.53)
Language English Spanish Other Unknown	1,255 (75.0) 209 (12.5) 117 (7.0) 93 (5.6)	12 1 1 1	1.0 (0.55, 1.66) 0.5 (0.01, 2.64) 0.9 (0.02, 4.67) 1.1 (0.03, 5.84)
Insurance Uninsured Public Private	804 (48.1) 768 (45.9) 102 (6.0)	7 8 0	0.9 (0.35, 1.79) 1.0 (0.54, 2.01) 0.0
Race/ethnicity White Black Latino Other Unknown	423 (25.3) 477 (28.5) 387 (23.1) 306 (18.2) 81 (4.9)	3 4 5 0 3	0.7 (0.15, 2.06) 0.8 (0.34, 2.13) 1.3 (0.42, 2.99) 0.0 3.7 (0.77, 10.44)
Homeless	304 (18.3)	6	2.0 (0.73, 4.25)
Unclassified ^b	34 (2.0)	1	2.9 (0.07, 15.33)
>1 visit to the ED during the study period	351 (21.1)	3	0.9 (0.18, 2.48)
Admitted to the hospital	844 (50.8)	4	0.5 (0.13, 1.21)
Total	1,674 (100.0)	15	0.8 (0.46, 1.40)

Table 2. Prevalence of unknown HIV infection among patients seeking care at the San Francisco General Hospital ED, March 2007

^aAge was missing for one patient.

^bUnclassified refers to patients for whom some basic information (first and last names) was lacking during the ED encounter.

HIV = human immunodeficiency virus

ED = emergency department

DISCUSSION

In our cross-sectional, unlinked HIV-prevalence study, we found that 0.9% of the patients seeking care at the SFGH ED had unknown HIV infection. While the overall prevalence of HIV infection in the population was approximately 9.0%, the relative prevalence of unknown HIV infection (approximately 10.0%) was lower than the national estimate of 25.0%. About one out of 10 HIV-infected individuals (10.0%) seeking care at the ED in our institution were HIV-infected and did not know it. Our findings contrast with previous reports suggesting that one-fourth to one-third of patients with HIV infection do not know their serostatus.^{2,29} However, our findings are more consistent with reports from a population-based study in San Francisco showing an

overall prevalence of nearly 0.8% of unknown HIV infection.³⁰ Indeed, our data suggest that using the prevalence of known HIV infection as a surrogate for the estimated prevalence of unknown HIV infection might lead to an overestimation of such prevalence in certain settings. Therefore, routine HIV-testing interventions among nonselected populations might turn out to be much less cost-effective than anticipated. Furthermore, the relatively modest prevalence of unknown HIV infection found in our study suggests either that HIV-infected individuals who are unaware of their infection use health-care services other than the ED in San Francisco or that previous estimates of their infection are too high.

Our study population consisted of patients with

Sar	ר Frai	ncisco	General H	ospital El	D, March 2	007									
				Dem	ographics			HIV test	ing history		Нe	ealth-care ser	vices used (p	rior 30 days	(
	Sex	Age	Race	Marital status	Language	Insurance	Homeless	HIV Ab	Tests rejected due to lack of consent	ED visits	UCC visits	Hospital admissions	Admission service	Length of hospital admission (in days)	Disposition
-	Σ	35	White	Single	English	Public	No			0	0	0			
2	Σ	23	Unknown	Single	Unknown	Uninsured	Yes			0	0	0			
m	Σ	49	Black	Single	English	Uninsured	Yes			~	-	0			
4	Σ	26	Hispanic	Single	English	Uninsured	No			0	0	0			
ß	Σ	47	Black	Single	English	Public/	No	March	July 2001	~	0	2	Medical	4	Home
				I	I	Medicaid		1999 Julv 2001	test reiected				Medical	Ω	Home
9	Σ	47	Unknown	Single	English	Public/	No			0	~	, -	Neuro-	23	Other facility
						Medicare							surgery		
7	ш		White	Single	Other	Uninsured	Unknown			0	0	0			
ø	Σ	52	Hispanic	Single	English	Uninsured	Yes	May 1999		0	ო	0			
6	Σ	27	Hispanic	Single	English	Public/ Other	No			0	0	0			
10	Σ	43	Black	Single	English	Public/ Medicaid	Yes			0	0	0			
1	Σ	24	Hispanic	Single	Spanish	Public	No			0	0	0			
12	Σ	27	Hispanic	Single	English	Uninsured/jail	Yes			0	0	0			
13	Σ	55	Unknown	Single	English	Uninsured	Unknown			0	0	, -	Medical	6	Home
14	Σ	51	White	Single	English	Public	Yes			œ	0	0			
$15^{\rm a}$	ш	58	Black	Widow	English	Public	No			0	0	0			
ªPat	ient di	agnosed	with acute F	HV infection	, HIV-1 viral l	oad was confirm	ed to be 78,0	00 copies/m	m³.						

Table 3. Summary of the characteristics of patients with unknown HIV infection at the

Public Health Reports / 2008 Supplement 3 / Volume 123

HIV = human immunodeficiency virus

ED = emergency department Ab = antibody

UCC = urgent care clinic

M = male F = female

blood samples taken for routine medical care seeking medical attention at the ED during a one-month period. The unlinked nature of our design allowed us to test for unknown HIV infection among 45% (1,674 out of 3,673 patients) of the patients seen at the ED during that interval, allowing the study of most subgroups of patients. By conducting an unlinked seroprevalence study, we avoided the selection bias generally introduced by studies of other designs, potentially increasing the generalizability of our results. Similarly, the relatively narrow 95% CIs around the point prevalence estimates of the entire sample and of most subgroups are a reflection of the size of the total sample and the distribution of the total sample across the different subgroups, and suggest the accuracy of our prevalence estimates.

While our sample reflects the demographic distribution of the patients seen at the ED during March 2007 (the study period) and that of calendar year 2006, given the nature of the design, our sample likely represents the sicker subgroup of those patients. As we would have expected, the patients included in our sample were more likely to be admitted to the hospital when compared with the entire population of patients seeking care at the ED. Thus, although we are confident that our estimates of unknown HIV infection reflect those of the population of patients getting blood drawn for medical care at the ED, it remains unknown if our results are generalizable to the entire population of patients seeking care at the SFGH ED. Furthermore, given that we only included one ED at a county hospital in San Francisco, our results might not be generalizable to other EDs in San Francisco or other cities.

Acute HIV infection in health-care settings may be more common than previously suspected. We found that approximately 7% (one of 15) of the patients with unknown HIV infection presenting to our ED had acute HIV infection. Consistent with our findings, a

Table 4. Selected risk factors for unknown	HIV infection among patients seeking care
at the San Francisco General Hospital ED,	March 2007

	Bivariate OR		Adjusted OR	_ /
	(95% CI)	P-value	(95% CI)	P-value
Gender				
Female	1.00			
Male	7.95 (1.04, 60.86)	0.046	7.68 (0.98, 60.26)	0.053
Age category (in years)				
>46	1.00			
31–45	0.76 (0.15, 3.76)	0.732	NS	NS
18–30	2.72 (0.83, 8.99)	0.100	3.15 (1.03, 9.61)	0.044
Race/ethnicity				
White	1.00			
Black	1.01 (0.24, 4.22)	0.995	NS	NS
Hispanic	2.07 (0.60, 7.19)	0.253	NS	NS
Language				
English	1.00			
Spanish	0.58 (0.08, 4.47)	0.599	NS	NS
Non-homeless	1.00			
Homeless	3.87 (1.29, 11.60)	0.016	3.89 (1.32, 11.45)	0.014
Insurance	1.00			
No insurance	1.09 (0.38, 3.12)	0.875	NS	NS
Not unclassified	1.00			
Unclassified	3.79 (0.48, 29.84)	0.205	NS	NS
	1.00			
More than one ED visit	1.00	0.901	NIC	NIC
Note than one ED visit	1.10 (0.50, 4.00)	0.071	113	113
No urgent care clinic visit	1.00			
Urgent care clinic visit	2.07 (0.27, 16.16)	0.488	NS	NS

HIV = human immunodeficiency virus

ED = emergency department

CI = confidence interval

NS = not significant

Public Health Reports / 2008 Supplement 3 / Volume 123

OR = odds ratio

study performed at an urgent care center in Boston found that 1% (five of 499) of patients presenting with flulike symptoms had acute HIV infection.²² Similarly, a different study found that when patients undergoing evaluation for mononucleosis with negative heterophile antibody tests were screened, 1% of them had acute HIV infection.²³ Unfortunately, acute HIV infection is rarely considered in the differential diagnosis of patients presenting to EDs, and no screening programs for acute HIV infection of patients seeking care at an ED exist in the U.S.³¹⁻³³ Our results suggest that patients with acute HIV infection might represent a significant proportion of the patients with unknown HIV infection presenting to EDs. Given the potential clinical and public health importance of identifying such patients, the yield and cost-effectiveness of routine, acute-HIV screening programs in EDs and urgent care settings should be evaluated.

Whether routine HIV screening is a cost-effective intervention to detect patients unaware of their HIV infection depends on the prevalence of unknown HIV infection in the population. A recent analysis showed that routine HIV screening is a cost-effective intervention in populations with HIV prevalence of 0.1%, suggesting that routine HIV screening might be a cost-effective measure in our setting.³⁴ However, the implementation of the Centers for Disease Control and Prevention's (CDC's) recent recommendations on HIV testing²⁴ without new resources or a reprioritization of existing allocations for HIV testing in busy health-care settings with rapid patient turnover is challenging.

The universal, opt-out, routine HIV screening recommended by CDC is likely to lead to the highest number of new HIV-infected patients detected; however, its implementation is not practical under current CDC funding priorities. The multiple barriers to the implementation of this screening strategy are discouraging to clinicians and public health officials, and preclude the implementation of other, simpler, less expensive, targeted HIV screening programs. Targeted HIV screening programs are based on risk factors for HIV infection and, therefore, will miss the diagnosis of HIV-infected individuals lacking those traditional risk factors until later in the course of their disease. However, if targeted, risk-based screening requires fewer resources, as it is often assumed, implementation and sustainability of such targeted screening programs might be more feasible. Furthermore, risk-based HIV screening might allow funds to be directed toward maintaining much-needed prevention case-management services, which studies have shown contribute to better diagnosis, lower transmission rates, and better treatment outcomes.^{3,35}

Central to targeted screening is the identification of risk factors. Traditional risk factors for HIV infection include injection drug use, unprotected anal or vaginal sexual intercourse with multiple sex partners, concurrent sexually transmitted infections, and lack of male circumcision. Nevertheless, risk factors vary widely depending on the geographic location and the population, and each ought to be evaluated to match a particular program to a population and maximize the diagnoses of HIV-infected patients. Consistent with the epidemiology of HIV-infected patients diagnosed late in the course of their disease in San Francisco, we found that unknown HIV-infected patients were more likely to be young men from underserved populations. In particular, we found that being male and being homeless were significantly associated with unknown HIV infection in the bivariate analysis. After adjusting for possible confounders in a multivariate model, being younger and being homeless were significantly associated with unknown HIV infection, with a strong but borderline association with being male. Interestingly, Hispanic patients with unknown HIV infection were significantly younger than other racial/ethnic groups, suggesting that the characteristics of patients with unknown HIV infection may vary across different subgroups of the population.

It is important to note, however, that using male sex, homelessness, and younger age as correlates of unknown HIV infection in the population studied might allow targeted screening. If we had implemented HIV screening targeting all homeless patients (men and women) and all men regardless of homelessness status during the study period, we would have detected 100% of the cases with unknown HIV infection by testing 65% of the population. Similarly, by targeting all people with either public health insurance (i.e., Medicare and Medicaid) or no insurance, we would have also detected all cases by testing 93% of our population. However, by restricting our HIV antibody testing to men with either public health insurance or no insurance, we would have detected 13 (93%) out of the 14 cases by testing only 58% of the population. Whether universal screening, with its associated higher costs and increased difficulties in program sustainability, should be implemented to detect the small number of unknown HIV-infected patients who belong to populations not targeted by risk-based screening is ultimately a choice to be determined by each institution and society.

In San Francisco, people diagnosed with AIDS within one year of their HIV diagnosis are more likely to belong to racial/ethnic minority groups, to have no reported risk for HIV infection, to be born outside of the U.S., and to be uninsured, among

other risk factors.8 Other studies have found similar characteristics of late testers in other U.S. cities.^{36,37} In our study, none of the unknown HIV-infected patients had evidence of recent infection by detuned EIA and, therefore, were likely to have chronic (not recent) HIV infection. Importantly, most patients with unknown HIV infection had multiple encounters with the health-care system during the three months prior to the study period and, in some cases, they were even admitted to the hospital. Those encounters clearly represented missed opportunities for diagnosing HIV infection. Our study did not allow us to determine the stage of HIV disease in those patients with unknown HIV infection. However, these results remind us of the potential impact of HIV testing of certain at-risk populations in health-care settings.

Limitations

Several limitations of our study should be acknowledged. The misclassification of individuals with previously diagnosed HIV infection as undiagnosed could have potentially led to an overestimation of the prevalence of patients with unknown HIV infection. We were particularly cautious in this regard and made a comprehensive effort to recognize previously diagnosed HIV-infected patients within our system. However, it was still possible that HIV-infected patients were diagnosed and received care outside the SFGH Medical Center system. Nevertheless, given that all our study patients utilized different health-care services at our institution regularly, it seems unlikely that no record of a previous diagnosis of HIV infection would exist in our system if either the health-care provider or the patient had known the diagnosis. In addition, in clinical practice, not all patients will disclose their known HIV status, and comprehensive review of medical records is unlikely to be standard in EDs. Therefore, a certain proportion of misclassification is also expected in clinical practice and in any HIV screening program.

Although related, the HIV seroprevalence of unknown HIV infection in any given population is not necessarily the same as the diagnostic yield of an HIV screening program implemented in such a population. Given that the latter one drives the determination of any cost-effectiveness of a screening program, any estimation of the cost-effectiveness of a program based on HIV seroprevalence remains speculative. We used electronic records and information collected for reasons other than this study, and it is possible that missing or inaccurate data led to misclassification of patients. However, we have no reason to believe that such misclassification was differential; therefore, it is unlikely to have introduced a significant bias to our results.

CONCLUSIONS

The relative prevalence of unknown HIV infection in our sample of patients from a county hospital ED was lower than expected from prior CDC estimates. However, acutely HIV-infected patients might represent a significant proportion of such patients. These findings suggest that targeted HIV screening strategies in our patient population might have higher diagnostic yield and decreased costs, and ultimately be more sustainable. Acute HIV screening in this setting might be of great clinical and public health importance. However, prospective studies are required to confirm this assertion.

Seroprevalence assessments are a valuable and underutilized tool to guide clinical and public health decisions. Further HIV seroprevalence studies in different populations would be highly valuable in guiding the implementation of HIV screening programs.

This study was carried out in part through the General Clinical Research Center at San Francisco General Hospital, supported by Grant 5-MO1-RR00083 from the Division of Research Resources, National Institutes of Health; by the California HIV Research Program Grant CH05-SMCHC-612; and by the San Francisco Department of Public Health.

REFERENCES

- Guidelines for national human immunodeficiency virus case surveillance, including monitoring for human immunodeficiency virus infection and acquired immunodeficiency syndrome. Centers for Disease Control and Prevention. MMWR Recomm Rep 1999;48 (RR-13):1–28.
- Glynn M, Rhodes P. Estimated HIV prevalence in the United States at the end of 2003 (abstract T1-B1101). Programs and abstracts of the 2005 National HIV Prevention Conference; 2005 Jun 12–15; Atlanta.
- Holtgrave DR. Costs and consequences of the US Centers for Disease Control and Prevention's recommendations for opt-out HIV testing. PLoS Med 2007;4:e194.
- Paltiel AD, Weinstein MC, Kimmel AD, Seage GR 3rd, Losina E, Zhang H, et al. Expanded screening for HIV in the United States an analysis of cost-effectiveness. N Engl J Med 2005;352:586-95.
- Hammer SM, Squires KE, Hughes MD, Grimes JM, Demeter LM, Currier JS, et al. A controlled trial of two nucleoside analogues plus indinavir in persons with human immunodeficiency virus infection and CD4 cell counts of 200 per cubic millimeter or less. AIDS Clinical Trials Group 320 Study Team. N Engl J Med 1997;337:725-33.
- Hulgan T, Raffanti S, Kheshti A, Blackwell RB, Rebeiro PF, Barkanic G, et al. CD4 lymphocyte percentage predicts disease progression in HIV-infected patients initiating highly active antiretroviral therapy with CD4 lymphocyte counts >350 lymphocytes/mm³. J Infect Dis 2005;192:950-7.
- Keruly JC, Moore RD. Immune status at presentation to care did not improve among antiretroviral-naive persons from 1990 to 2006. Clin Infect Dis 2007;45:1369-74.
- Schwarcz S, Hsu L, Dilley JW, Loeb L, Nelson K, Boyd S. Late diagnosis of HIV infection: trends, prevalence, and characteristics

of persons whose HIV diagnosis occurred within 12 months of developing AIDS. J Acquir Immune Defic Syndr 2006;43:491-4.

- Castilla J, Sobrino P, De La Fuente L, Noguer I, Guerra L, Parras F. Late diagnosis of HIV infection in the era of highly active antiretroviral therapy: consequences for AIDS incidence. AIDS 2002; 16:1945-51.
- Schwarcz S, Weinstock H, Louie B, Kellogg T, Douglas J, Lalota M, et al. Characteristics of persons with recently acquired HIV infection: application of the serologic testing algorithm for recent HIV seroconversion in 10 US cities. J Acquir Immune Defic Syndr 2007; 44:112-5.
- Missed opportunities for earlier diagnosis of HIV infection—South Carolina, 1997–2005. MMWR Morb Mortal Wkly Rep 2006; 55(47):1269-72.
- Battegay M, Fluckiger U, Hirschel B, Furrer H. Late presentation of HIV-infected individuals. Antivir Ther 2007;12:841-51.
- McDonald EA, Currie MJ, Bowden FJ. Delayed diagnosis of HIV: missed opportunities and triggers for testing in the Australian Capital Territory. Sex Health 2006;3:291-5.
- Cunningham CÓ, Sohler NL, Wong MD, Relf M, Cunningham WE, Drainoni ML, et al. Utilization of health care services in hard-toreach marginalized HIV-infected individuals. AIDS Patient Care STDS 2007;21:177-86.
- Alpert PL, Shuter J, DeShaw MG, Webber MP, Klein RS. Factors associated with unrecognized HIV-1 infection in an inner-city emergency department. Ann Emerg Med 1996;28:159-64.
- Rothman RE. Current Centers for Disease Control and Prevention guidelines for HIV counseling, testing, and referral: critical role of and a call to action for emergency physicians. Ann Emerg Med 2004;44:31-42.
- Kelen GD, Hexter DA, Hansen KN, Humes R, Vigilance PN, Baskerville M, et al. Feasibility of an emergency department-based, risk-targeted voluntary HIV screening program. Ann Emerg Med 1996;27:687-92.
- Brown J, Shesser R, Simon G. Establishing an ED HIV screening program: lessons from the front lines. Acad Emerg Med 2007; 14:658-61.
- Lyss SB, Branson BM, Kroc KA, Couture EF, Newman DR, Weinstein RA. Detecting unsuspected HIV infection with a rapid whole-blood HIV test in an urban emergency department. J Acquir Immune Defic Syndr 2007;44:435-42.
- Rothman RE, Ketlogetswe KS, Dolan T, Wyer PC, Kelen GD. Preventive care in the emergency department: should emergency departments conduct routine HIV screening? A systematic review. Acad Emerg Med 2003;10:278-85.
- Zetola NM, Pilcher CD. Diagnosis and management of acute HIV infection. Infect Dis Clin North Am 2007;21:19-48, vii.
- Pincus JM, Crosby SS, Losina E, King ER, LaBelle C, Freedberg KA. Acute human immunodeficiency virus infection in patients presenting to an urban urgent care center. Clin Infect Dis 2003; 37:1699-704.
- Rosenberg ES, Caliendo AM, Walker BD. Acute HIV infection among patients tested for mononucleosis. N Engl J Med 1999;340:969.

- Branson BM, Handsfield HH, Lampe MA, Janssen RS, Taylor AW, Lyss SB, et al. Revised recommendations for HIV testing of adults, adolescents, and pregnant women in health-care settings. MMWR Recomm Rep 2006;55(RR-14):1-17.
- Rothman RE, Lyons MS, Haukoos JS. Uncovering HIV infection in the emergency department: a broader perspective. Acad Emerg Med 2007;14:653-7.
- Janssen RS, Satten GA, Stramer SL, Rawal BD, O'Brien TR, Weiblen BJ, et al. New testing strategy to detect early HIV-1 infection for use in incidence estimates and for clinical and prevention purposes. JAMA 1998;280:42-8.
- Kothe D, Byers RH, Caudill SP, Satten GA, Janssen RS, Hannon WH, et al. Performance characteristics of a new less sensitive HIV-1 enzyme immunoassay for use in estimating HIV seroincidence. J Acquir Immune Defic Syndr 2003;33:625-34.
- SAS Institute Inc. SAS: Version 9.1. Cary (NC): SAS Institute Inc.; 2003.
- HIV prevalence, unrecognized infection, and HIV testing among men who have sex with men—five U.S. cities, June 2004–April 2005. MMWR Morb Mortal Wkly Rep 2005;54(24):597-601.
- Schwarcz S, Scheer S, McFarland W, Katz M, Valleroy L, Chen S, et al. Prevalence of HIV infection and predictors of high-transmission sexual risk behaviors among men who have sex with men. Am I Public Health 2007;97:1067-75.
- Daar ES, Little S, Pitt J, Santangelo J, Ho P, Harawa N, et al. Diagnosis of primary HIV-1 infection. Los Angeles County Primary HIV Infection Recruitment Network. Ann Intern Med 2001;134:25-9.
- Sherlock M, Zetola NM, Klausner JD. Routine detection of acute HIV infection through RNA pooling: survey of current practice in the United States. Sex Transm Dis 2007;34:314-6.
- Weintrob AC, Giner J, Menezes P, Patrick E, Benjamin DK Jr., Lennox J, et al. Infrequent diagnosis of primary human immunodeficiency virus infection: missed opportunities in acute care settings. Arch Intern Med 2003;163:2097-100.
- Patel P, Klausner JD, Bacon OM, Liska S, Taylor M, Gonzalez A, et al. Detection of acute HIV infections in high-risk patients in California. J Acquir Immune Defic Syndr 2006;42:75-9.
- Kamb ML, Fishbein M, Douglas JM Jr., Rhodes F, Rogers J, Bolan G, et al. Efficacy of risk-reduction counseling to prevent human immunodeficiency virus and sexually transmitted diseases: a randomized controlled trial. Project RESPECT Study Group. JAMA 1998;280:1161-7.
- Levy V, Prentiss D, Balmas G, Chen S, Israelski D, Katzenstein D, et al. Factors in the delayed HIV presentation of immigrants in Northern California: implications for voluntary counseling and testing programs. J Immigr Minor Health 2007;9:49-54.
- Kellerman SE, Lehman JS, Lansky A, Stevens MR, Hecht FM, Bindman AB, et al. HIV testing within at-risk populations in the United States and the reasons for seeking or avoiding HIV testing. J Acquir Immune Defic Syndr 2002;31:202-10.