AIDS PATIENT CARE and STDs
Volume 21, Number 3, 2007

DOI: 10.1089/apc.2006.0097

Predictors of Delayed HIV Diagnosis in a Recently Diagnosed Cohort

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ABSTRACT

Delayed diagnosis of HIV is associated with a worse prognosis despite highly active antiretroviral therapy. Many persons with HIV infection are diagnosed late in the disease process. We conducted a study of 119 persons recently diagnosed with HIV infection to determine the association of health literacy and other factors with delayed diagnosis. Patients were recruited from four publicly funded facilities in Houston, Texas. Health literacy was measured with the Test of Functional Health Literacy in Adults (TOFHLA). Delayed diagnosis was assessed by CD4 cell count at diagnosis. Sixty-five percent of patients had CD4 cell counts 350 cells/mm^3 or less. Twenty-eight percent had inadequate health literacy, but literacy was not associated with CD4 cell count. Thirty-eight percent were tested because they "felt sick." In multivariable analysis, female gender ($p = 0.005$), reason tested other than "felt sick" ($p < 0.001$), and marijuana use ($p = 0.004$) and other illicit drug use ($p = 0.01$) were predictors of having a higher CD4 cell count at diagnosis. These results confirm that late diagnosis of HIV is common among users of public health care facilities. Expanded routine testing for HIV infection is needed with attention directed to men and persons who may not recognize that they are at risk for contracting HIV infection.

INTRODUCTION

Of the 1.1 million people in the United States infected with HIV, approximately one-quarter are unaware of their infection, even after two decades of HIV awareness campaigns and education.[1] Despite the fact that treatment of HIV infection can dramatically prolong life, a CD4 cell count less than 200 cells/mm^3 or an AIDS-defining illness at diagnosis is still associated with a worse prognosis.[2] Unfortunately, many persons who have been diagnosed with HIV infection were diagnosed late in the course of their disease. A study from the US Centers for Disease Control and Prevention (CDC) of 2441 persons with AIDS found that 36% first tested positive for HIV within 2 months of being diagnosed with AIDS and another 15% were diagnosed with HIV within 3–12 months of being diagnosed with AIDS.[3] The study was based on data from 1990–1992, and evaluated a limited number of

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factors as predictors of late diagnosis. It found that persons exposed to HIV from injection drug use or heterosexual contact, with less education, and who were black or Hispanic were more likely to be diagnosed late in their disease. Samet et al.[4] conducted a comprehensive assessment of patients diagnosed just before the advent of highly active antiretroviral therapy (HAART). The median initial CD4 cell count in that cohort of 203 patients was 280 cells/mm^3, and male gender, older age, and no history of jail time were associated with lower CD4 cell counts. Dybul et al.[5] evaluated the initial CD4 cell counts of 2223 people diagnosed in 1999–2000 and found that 57% had CD4 cell counts less than 350 cell/mm^3 and 36% had CD4 cell counts less than 200 cells/mm^3. The study could only examine gender and race as predictors of delayed diagnosis and found no clear differences by gender or race. These studies indicate that delayed diagnosis was common in the pre-HAART and early HAART eras. They suggest that gender, education, race, HIV risk factor, and socioeconomic status may be associated with delayed diagnosis of HIV infection. Persons with HIV infection in the pre-HAART and early HAART eras may have delayed testing for HIV because of little perceived benefit from knowing one's status. Whether these same or other factors are important in the current era of highly effective therapy is not known.

According to the National Adult Literacy Survey of over 26,000 adults, approximately 40–44 million (21%–23%) adults in the United States were functionally illiterate, and an additional 50 million (25%–28%) adults were marginally literate.[6] Minorities, older adults, and those with less than a high school education tended to perform in the lower literacy levels.[6] Low literacy has been associated with poorer health outcomes.[7] Health literacy is a type of literacy that has been defined as "the degree to which individuals have the capacity to obtain, process and understand basic health information and services for appropriate health decisions."[8] A survey of 2659 indigent and minority patients at two large county hospitals in the United States found that an alarming percent of patients were unable to perform basic health care related tasks: 60% did not understand an informed consent, 42% did not understand how to take medication on an empty stomach, and 26% did not understand when their next appointment was after reading an appointment slip.[9] It has been noted that some informational HIV/AIDS brochures have been written at levels too advanced for their intended audience.[10] While literacy and health literacy are not interchangeable, it would be difficult to have adequate health literacy without basic literacy skills.

We sought to examine the factors associated with delayed diagnosis of HIV infection in a recently diagnosed population. Given the prevalence of low literacy and low health literacy in the United States and the frequency of delayed diagnosis of HIV infection, we posited that delayed diagnosis may be in part due to inadequate health literacy. We reasoned that persons with inadequate health literacy are less knowledgeable about HIV infection, specifically about modes of transmission, and are therefore less likely to seek testing. We also determined if other factors were associated with CD4 cell count at diagnosis, and selected these based on the Health Belief Model.[11] To our knowledge the possible link between severity of HIV at diagnosis and health literacy has not been evaluated. We tested the hypothesis that poorer health literacy was associated with low CD4 cell count at the time of diagnosis of HIV infection.

MATERIALS AND METHODS

Study design and subjects

A convenience sample of 149 subjects was recruited from four publicly funded facilities for HIV-infected persons in Houston, Texas: the Thomas Street Health Center, the Northwest Health Center, the Michael E. DeBakey VA Medical Center, and the Ben Taub General Hospital. These sites provide care for 25% of the persons in care for HIV in Harris County, Texas, and 50% of the uninsured patients in care in Harris County. Patients diagnosed with HIV infection within the past 3 years were eligible for the study. Patients were referred to the study by physicians, nurses, or social work-

ers and were excluded if they were younger than 18 years old, blind, too sick to participate, unable to communicate in English or Spanish, did not receive care at one of the participating health care centers, were evacuees from New Orleans, Louisiana (because their CD4 cell count from diagnosis would not be retrievable), or were known to have a neurocognitive deficit that would preclude them from reliably completing the survey.

Instruments and variable definitions

The outcome variable, initial CD4 cell count, was abstracted from medical records and was defined as the first CD4 cell count recorded after the diagnosis of HIV infection. A CD4 cell count obtained within six months of diagnosis was used if the initial CD4 cell count could not be retrieved so long as the patient was HAART naive at the time of that laboratory testing.

The main explanatory variable of interest, health literacy, was obtained from a validated self-administered survey, the Test of Functional Health Literacy in Adults (TOFHLA).[12] The TOFHLA is composed of two parts, a numeracy comprehension assessment and a reading comprehension assessment. The test is scored from 0 to 100 with 0 to 59 representing inadequate health literacy, 60 to 74 representing marginal health literacy, and 75 to 100 representing adequate health literacy. Patients were dichotomized as having either inadequate health literacy (0 to 74) or adequate health literacy (75 to 100).

Potential confounders to the relationship between health literacy and CD4 cell count at diagnosis of HIV infection were chosen based on the Health Belief Model.[11] Sociodemographic variables included age, race, ethnicity, gender, education, sexual orientation, and HIV risk factor. "Perceived susceptibility" included perceived susceptibility to contracting HIV and HIV knowledge. "Cues to action" included reason tested for HIV. "Perceived barriers" included perceived access to care, substance abuse, and trust in the health care system. Perceived benefits to testing and general self-efficacy were also evaluated. We used validated instruments to assess perceived access to care,[13] and general self-efficacy.[14] We also assessed trust in the health care system, perceived benefits of testing, HIV knowledge, cues to HIV testing, and perceived susceptibility to HIV infection with scales developed by the study team. Item responses for newly developed scales were assessed for their levels of interitem correlations (acceptable range, 0.2–0.9). Unidimensional factor models were confirmed for each scale, noncontributing or redundant items were removed, and summary scale scores were calculated. All survey items except the TOFLHA were interviewer-administered.

Data analysis

Initial CD4 cell counts were stratified into three categories (0–200 cell/mm^3, 201–350 cells/mm^3, >350 cells/mm^3) based on clinical parameters and cross-tabulated with health literacy. Continuous explanatory variables were dichotomized at the median for the purposes of obtaining the median CD4 cell count and interquartile range in each group, though they were left as continuous variables for the statistical testing. Univariable and multivariable statistical testing was accomplished with linear regression, using CD4 cell counts as the outcome variable. CD4 cell counts were natural log-transformed in the regression analyses to help normalize the data. Explanatory variables with a $p < 0.25$ in the univariable regression analysis were placed into a multivariable regression model. Each explanatory variable was selectively removed at $p > 0.10$ to determine the final model. All reported p values are two-sided. All statistics were analyzed with Stata V 8.0 (Stata Press, College Station, TX).

Human subjects

The study was approved by the Institutional Review Board for Baylor College of Medicine and Affiliated Hospitals. All subjects gave written informed consent.

RESULTS

There were 149 patients enrolled in the study. Twenty patients met one of the exclusion criteria (17 were diagnosed more than 3 years before enrollment and 3 were not patients

at one of the participating sites), 2 did not complete the interview, and 1 withdrew consent. For 23 of the remaining 126 patients, the initial CD4 cell count could not be retrieved, but we were able to retrieve a CD4 cell count within 6 months of diagnosis and before the patient was treated with HAART for 16 patients. A qualifying CD4 cell count could not be obtained for 7 patients. The final analysis was performed on 119 patients.

Twenty-nine percent presented with CD4 cell counts of 50 cells/mm^3 or less, 21% with counts between 51–200, 15% with counts between 201–350, and 35% with counts more than 350. Additional baseline characteristics of the patients are presented in Table 1. Of note, 36% of the patients were female, more than half of the patients were black, and 28% identified themselves as Hispanic. Sixty-nine percent identified themselves as heterosexuals, and the majority of patients acquired HIV through sexual intercourse. Twenty-eight percent never completed high school, while 29% had some college education. Most subjects reported that they believed they were susceptible to contracting HIV. Thirty-eight percent were tested for HIV because they "felt sick" rather than for some other reason. Fifty-four percent were diagnosed with HIV infection in the past year and 43% were diagnosed in the hospital. The median CD4 cell count at diagnosis was 206 cells/mm^3 (range, 2–1456; interquartile range, 35–478).

Twenty-eight percent of the sample had inadequate health literacy. The distribution of literacy level by CD4 cell count group is presented in Table 2. The majority of patients in each CD4 cell category had adequate health literacy. Persons with inadequate health literacy had a somewhat lower mean CD4 cell count at diagnosis (median, 175; interquartile range, 69, 272) than persons with adequate health literacy (median, 247; interquartile range, 31, 517), but this difference was not statistically significant ($p = 0.75$; Table 1). Gender, reason tested for HIV, perceived access to care, illicit drug use, and marijuana use were all statistically significantly associated with CD4 cell count at diagnosis of HIV infection. Multivariable linear regression was performed to assess variables associated with a higher CD4 cell count at diagnosis (Table 3). A higher CD4 cell count at diagnosis was associated with female gender, reason tested for HIV other than "felt sick," and marijuana use. After back transforming the regression coefficients, women had 123% higher CD4 cell counts at diagnosis than men ($p = 0.005$). Subjects who were tested for HIV for reasons other than being sick had 232% higher CD4 cell counts at diagnosis ($p < 0.001$), whereas persons who did not report marijuana use had 57% lower CD4 cell counts at diagnosis ($p = 0.004$). Marijuana use correlated with the use of other illicit substances, with 76% of marijuana users also reporting other illicit drug use. Separate multivariable models that considered other illicit drug use, but did not include marijuana use, found that other illicit drug use was an independent predictor of earlier diagnosis of HIV ($p = 0.01$) (data not shown). Health literacy was not associated with CD4 cell count at diagnosis. Interaction terms representing race and gender, health literacy, and reason tested, and health literacy and gender were also not significantly associated with initial CD4 cell count in separate analyses.

DISCUSSION

In this study of 119 patients in care for HIV in publicly funded hospitals and clinics in Houston, Texas, we evaluated whether health literacy was a predictor of delayed diagnosis of HIV infection as measured by CD4 cell count at diagnosis. Half of the patients had an AIDS-defining CD4 cell count at diagnosis and 65% were immunosuppressed enough to warrant treatment (CD4 cell count <350 cells/mm^3),[15] indicating they were tested late in the disease course. We hypothesized that inadequate health literacy would be a predictor of delayed testing and that patients with inadequate health literacy would have lower CD4 cell counts at diagnosis. This hypothesis was not supported by the data. Our study did find, however, that gender, reason tested, and marijuana use were all independent predictors of higher CD4 cell count at diagnosis.

To our knowledge this is the first study to explore the association between health literacy and

TABLE 1. BASELINE CHARACTERISTICS AND UNIVARIABLE ANALYSIS OF FACTORS ASSOCIATED WITH CD4 CELL COUNT AT DIAGNOSIS AMONG ONE HUNDRED NINETEEN PATIENTS DIAGNOSED WITH HIV WITHIN THIRTY-SIX MONTHS

Characteristics	n *(%)*	*Median CD4 cell count (cell/mm^3)*	*Interquartile range*	p *value*[b]
Demographic/socioeconomic characteristics				
Age				0.06
18–29	26 (22)	237	32, 540	
30–39	33 (28)	96	32, 378	
40–49	41 (34)	197	31, 361	
> 50	19 (16)	374	128, 595	
Gender				0.01
Male	76 (64)	144	32, 368	
Female	43 (36)	349	116, 646	
Race				0.58
Black	63 (53)	175	32, 478	
White	39 (33)	240	38, 520	
Other/multiple	17 (14)	206	89, 412	
Ethnicity				0.74
Hispanic	33 (28)	128	38, 331	
Not Hispanic	86 (72)	247	35, 517	
Sexual Orientation				0.44
Gay/lesbian	28 (24)	237	78, 470	
Heterosexual	82 (69)	202	34, 490	
Other	9 (8)	160	11, 406	
Education				0.09
Never finished high school	33 (28)	197	35, 595	
High school diploma or GED	51 (43)	245	69, 490	
Some higher education	35 (29)	105	15, 357	
HIV risk factor				0.78
Men who have sex with men (MSM)	33 (28)	172	35, 374	
Any injection drug use (IDU)	15 (13)	213	26, 645	
Heterosexual intercourse	71 (60)	219	36, 490	
Perceived Susceptibility				
Perceived susceptibility to contracting HIV				0.18
Yes	111 (93)	206	38, 474	
No	8 (7)	113	9, 557	
HIV knowledge[a] (n = 109) (possible score 0–11)	11 (7,11)[c]			0.11
< median	41 (38)	191	26, 408	
≥ median	68 (62)	260	42, 523	
Self-efficacy				
Self-efficacy[a] (n = 111) (possible score 6–36)	24 (11, 36)[c]			0.13
< median	48 (43)	227	88, 549	
≥ median	63 (57)	219	25, 408	
Cues to Action				
Reason tested for HIV				<0.001
Felt sick	45 (38)	69	11, 300	
Other[d]	74 (62)	265	96, 558	
Perceived Barriers				
Perceived access to care[a] (n = 110) (possible score 6–36)	27 (11, 36)[c]			0.05
< median	52 (47)	294	78, 595	
≥ median	58 (53)	124	23, 374	
Substance Use (lifetime)				
Illicit drug user (n = 114)				
Yes	64 (56)	299	88, 531	0.04
No	50 (44)	118	18, 378	
Marijuana use (n = 118)				0.002
Yes	75 (64)	257	87, 540	
No	43 (36)	96	12, 312	
Alcohol use (n = 118)				0.65
Yes	103 (83)	219	36, 525	
No	15 (13)	160	34, 374	

(*continued*)

TABLE 1. BASELINE CHARACTERISTICS AND UNIVARIABLE ANALYSIS OF FACTORS ASSOCIATED WITH CD4 CELL COUNT AT DIAGNOSIS AMONG ONE HUNDRED NINETEEN PATIENTS DIAGNOSED WITH HIV WITHIN THIRTY-SIX MONTHS (*CONTINUED*)

Characteristics	n *(%)*	*Median CD4 cell count (cell/mm^3)*	*Interquartile range*	p *value*[b]
Trust in the health care system[a] (possible score 4–20)	17 (7, 20)[c]			0.30
< median	53 (45)	248	81, 517	
≥ median	66 (55)	143	34, 406	
Perceived benefits				
Perceived benefits of testing[a] (n = 117) (possible score 4–24)	22 (4, 24)[c]			0.63
< median	51 (44)	197	32, 478	
≥ median	66 (56)	200	36, 490	
Health literacy				0.75
Inadequate	33 (28)	175	69, 272	
Adequate	86 (72)	247	31, 517	
Time since HIV diagnosis				0.07
< 6 months	44 (37)	172	24, 449	
6–12 months	20 (17)	140	30, 234	
> 12–24 months	29 (24)	312	60, 594	
> 24–36 months	26 (22)	237	110, 474	
Diagnosis location				0.09
Inpatient	51 (43)	147	25, 357	
Outpatient	68 (57)	249	53, 519	

[a]Left as continuous for univariable and multivariable regressions; characteristic incrases as value increases.
[b]p values from univariable regressions of log transformed CD4 cell counts.
[c]Median (range).
[d]Other reasons for testing included: recommended by a health care profesional, thought might have been infected, recommended by a friend, family member, or sex partner, because they knew someone with HIV, recommended by the health department, because of blood donation, and other reasons.
[e]Illicit substances included: methamphetamine, cocaine, crack, free base, inhalants, LSD/other hallucinogens, or heroin
GED, General Equivalency Diploma.

HIV testing behaviors. Poor health literacy has been related to less adherence to antiretroviral medications.[16] Previous studies evaluating health literacy as a predictor of screening behaviors have shown mixed results. Guerra et al.[17] found that health literacy did not predict colorectal screening. Inadequate health literacy, however, was predictive of failure to receive Papanicolaou smears, mammograms, and influenza and pneumococcal vaccinations in older Medicare patients.[18] Why these inconsistent results have been obtained is not clear. Nearly all the subjects in the present study tested late in the course of their HIV infection, and were driven to seek HIV testing by symptoms or external recommendations. It is possible that any effect of health literacy on HIV testing behavior may be overwhelmed by barriers to HIV testing, such as fear, stigma, and poor access to health care.[19–21] It is also possible that the TOFHLA is not an accurate measure of health literacy, and that literacy, not health literacy, was tested.[22] Regardless, the high frequency of delayed diagnosis, coupled with the fact that it was not associated with poor health literacy, suggest that written materials either do not reach or do not influence their intended target population. Current efforts to encourage HIV testing have limited effectiveness in the uninsured persons represented by this study popu-

TABLE 2. HEALTH LITERACY STRATIFIED BY CD4 CELL COUNT AT DIAGNOSIS OF HIV (N = 119)

	CD4 cell count (cells/mm^3) n *(%)*		
Health literacy	0–200	201–350	> 350
Inadequate	20 (33)	6 (33)	7 (17)
Adequate	39 (66)	12 (66)	35 (83)

Table 3. Multivariable Linear Regression Model of Log Transformed CD4 Cell Count at Diagnosis of HIV Infection ($N = 118$)

Characteristics	*Coefficient*	*95% confidence limit*	p *value*	*% change*[a]
Gender				
Male	Referent group			
Female	0.80	0.24, 1.36	0.005	123
Health literacy				
Inadequate	Referent group			
Adequate	−0.28	−0.88, 0.32	0.35	−24
Reason tested				
Felt sick	Referent group			
Other	1.20	0.64, 1.76	< 0.001	232
Marijuana (lifetime)				
Yes	Referent group			
No	−0.85	−1.41, −0.28	0.004	−57

[a]Estimated % change in CD4 cell count at diagnosis of HIV infection compared to the referent group, adjusted for all other variables in the table.

lation. Further research is needed to better understand these relationships, the impact of health literacy on health-related behavior, and whether changing health literacy is possible and efficacious at improving health outcomes.[23]

Men had a lower CD4 cell count at diagnosis than women, consistent with many previous studies.[4,24,25] One possible explanation for these findings is that women are offered testing in pregnancy.[26] Our study, however, only included three women who were diagnosed during a pregnancy. Men also generally utilize health care less and have less access to health care and health insurance than women, although in the present study nearly all of the participants were uninsured at the time of diagnosis.[27,28] Interventions to promote HIV testing may need to more aggressively target men, especially in environments other than the health care setting.

Forty-three percent of our patients were diagnosed during a hospitalization. Participants who were tested for HIV because they "felt sick" had CD4 cell counts that were about a quarter of those of participants tested for other reasons. A study by the CDC found that 65% of late testers tested because of an illness, whereas only approximately 20% of early testers tested because of an illness.[29] Many patients, especially minorities, fail to perceive their risk for HIV infection, while Kuo et al. found that health care providers may have missed opportunities to diagnose HIV earlier in a substantial portion of patients because they did not screen for high risk behavior or recognize signs and symptoms of HIV infection.[30,31] HIV screening in low prevalence populations is cost effective and may even be cost effective in the general population.[32,33] Our findings support the need for routine screening for HIV infection, at least among persons who are under-insured or uninsured. Rapid HIV testing may also lead to earlier diagnosis in this population because it can be used in urgent care and emergency room settings—settings often used by the underinsured and uninsured but that have typically avoided performing standard HIV testing because of the difficulties ensuring follow-up to deliver test results.[34]

The use of marijuana and other illicit substances was correlated with earlier diagnosis of HIV infection. This finding is counterintuitive. One can postulate that persons who use any of these illicit substances recognize themselves or are recognized by health care providers as members of a high-risk group and are therefore diagnosed earlier in the disease process. The obverse of this finding, that persons who do not use illicit substances are diagnosed later, suggests that HIV testing and education need to be directed toward individuals without this risk factor for HIV infection.

Interestingly, neither race nor ethnicity was a significant predictor of CD4 cell count at diagnosis, consistent with a previously conducted study at the Thomas Street Health Center.[35] These data are in contrast to CDC data

which show that Hispanic and black persons are diagnosed with HIV later than white persons.[3,25] The CDC data are not adjusted for income and insurance status, which likely differ by race/ethnicity. In contrast, the patients in the present study had similarly low income and lack of insurance regardless of race/ethnicity. Our data do not provide evidence that race or ethnicity directly influence CD4 cell count at diagnosis. They suggest that in the CDC data, race and ethnicity are markers for unmeasured factors associated with delayed diagnosis that differ by race/ethnicity, such as access to care, insurance status, and income. That hypothesis has not been tested.

This study has to be interpreted in light of its limitations. The cross-sectional study design does not allow assessment for a causal relationship between the predictors and outcome. The majority of patients were not newly diagnosed at the time of the survey and may have been in care for up to 3 years. This time in care may have influenced some of the predictors we studied. We also assumed that health literacy did not change with time, but cumulative exposure to the health care system could have improved participants' health literacy. We were not able to obtain complete information regarding history of AIDS-defining illnesses at time of diagnosis. Even though we attempted to exclude patients with neurocognitive disease, it is also possible that some patients had subclinical AIDS dementia, which could have affected their performance on the TOFHLA. The sample size was relatively small, and a larger study might have yielded a significant association between health literacy and CD4 cell count at diagnosis. Last, as a convenience sample the population studied over-represents persons who enter and remain in health care for HIV, which limits generalizability.[36,37]

CONCLUSIONS

In this study of 119 HIV-infected patients who receive care in publicly funded facilities in Houston, Texas, we evaluated whether health literacy was a predictor of delayed diagnosis of HIV infection as measured by CD4 cell count at time of diagnosis. Late diagnosis of HIV was common among users of public health care facilities, with 65% of the participants in this study immunocompromised enough at diagnosis to warrant HAART. Contrary to our hypothesis, health literacy was not a predictor of delayed diagnosis. Women, patients who were tested for reasons other than being sick, and persons who used illicit substances had higher CD4 cell counts at diagnosis. Prospective studies are needed to identify predictors of delayed diagnosis of HIV infection. Expanded routine testing for HIV infection is needed, with attention directed to men and persons who may not recognize that they are at risk for contracting HIV infection.

ACKNOWLEDGMENTS

The authors would like to thank Sallye M. Stapleton and Erick Villareal for their help in conducting the interviews. Supported by the National Institutes of Mental Health, National Institutes of Health (Grant K23MH067505), the Agency for Healthcare Quality and Research (Grant T32HP10031), and the facilities and resources of the Michael E. DeBakey Veterans Affairs Medical Center and the Harris County Hospital District, Houston, TX.

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