Published in final edited form as:

Am J Med. 2007 April ; 120(4): 370–373. doi:10.1016/j.amjmed.2006.05.050.

Late Diagnosis of HIV Infection: the Role of Age and Gender

Michael J. Mugavero, MD¹, Chelsea Castellano, BS¹, David Edelman, MD, MHS², and Charles Hicks, MD¹

¹Division of Infectious Diseases and International Health, Department of Medicine, Duke University

²Center for Health Services Research in Primary Care, Durham VA Medical Center

³Division of General Internal Medicine, Department of Medicine, Duke University

Abstract

Background—Late diagnosis of HIV infection is detrimental to infected persons and to the public health. The objective of this study was to identify factors associated with late diagnosis of HIV infection, defined as an initial CD4 T lymphocyte count < 200 cells/μL, in a cohort of recently diagnosed persons. Additionally, we evaluated factors associated with HIV infection being diagnosed during hospitalization.

Design—Cross-sectional study of a university-based HIV clinic in the southeastern U.S. Patients with newly diagnosed HIV infection evaluated at the Duke University HIV clinic between October 2002 and August 2004 were included in this analysis. Socio-demographic variables, site of HIV diagnosis, opportunistic infections present at diagnosis, initial CD4 T lymphocyte count and initial HIV RNA level were recorded for study subjects.

Results—49% of subjects met the immunologic definition of AIDS at the time of HIV diagnosis (CD4 count < 200 cells/μL). In multivariable logistic regression analyses, older patients were more likely to be diagnosed with a CD4 count < 200 cells/μL (OR=1.72, 95% CI= 1.12,2.64, p=0.01), and older patients (OR=1.79, 95% CI= 1.07,3.12, p=0.03) and women (OR=6.74, 95% CI= 2.08,21.81, p=0.001) were more likely to be diagnosed during hospitalization.

Conclusions—Late diagnosis of HIV infection is a considerable problem, particularly for older patients. Inpatient diagnosis of HIV infection is significantly more common among women and older patients. Improved HIV testing strategies may allow for more timely diagnosis of HIV infection, which may benefit both the infected individual and society.

Keywords

HIV; AIDS; Prevention; Diagnosis; Rural; South

Introduction

Highly active antiretroviral therapy (HAART) has proven effective in reducing morbidity and mortality associated with human immunodeficiency virus (HIV) infection.¹ Despite increased availability of HAART in the United States many HIV-infected persons do not fully benefit from therapy due to late diagnosis. Approximately 25% of the estimated 1.1

Corresponding author: Charles Hicks, MD; Division of Infectious Diseases and International Health; Duke University Medical Center Box 3360, Durham NC 27710; telephone: (919) 684-4474, fax: (919) 681-7494, charles.hicks@duke.edu.

Conflict of Interest Notification

The authors have no conflicts of interest to disclose relevant to this paper.

million persons living with HIV in the United States are unaware they are HIV-infected.² As a result, these persons do not achieve full benefit from life-prolonging antiretroviral and prophylactic medications. Recent data from the Centers for Disease Control and Prevention (CDC) indicate that approximately half the persons meeting the case definition for AIDS had been diagnosed with HIV infection less than a year before their AIDS diagnosis.³ Of all persons diagnosed with HIV infection in the U.S. in 2001, 39% progressed to AIDS within 12 months of their positive HIV test.⁴

This late diagnosis of HIV infection is detrimental both to the individual and to society. HIV-infected patients whose CD4 counts are below 200 cells/ μ L experience increased morbidity and mortality.⁵ Additionally, diminished responses to antiretroviral therapy and higher health care expenditures are the norm for HIV-infected persons with lower CD4 counts.⁵⁻⁷ There has been a recent focus on incorporating prevention of transmission strategies into the medical care of persons living with HIV, and trials have shown that focusing prevention counseling on HIV-infected persons reduces rates of high-risk sexual behaviors that might transmit HIV.^{8,9} Thus, early diagnosis of HIV infection has become increasingly important on many levels.

Studies assessing factors associated with late presentation for HIV care suggest older age and male gender are associated with late entry to care in some studies but not in others.¹⁰⁻¹² Most studies have focused on patients living in large urban settings in the Northeast and West. However, the South has the highest rates of new HIV infections and is home to 39% of persons living with AIDS in the U.S.¹³ Additionally, the socio-demographic characteristics of HIV-infected patients in the South differ from those observed in other regions of the country; over two thirds of patients diagnosed with AIDS in 2003 and residing in non-metropolitan areas live in the South.¹⁴ A study done over a decade ago showed that only 12% of recently diagnosed HIV-infected patients in South Carolina had CD4 T lymphocyte counts < 200 cells/ μ L,¹⁵ suggesting late diagnosis was relatively infrequent. Much has changed in the past 10 years regarding features of persons living with HIV/AIDS, including increased prevalence rates among African-Americans, Latinos, and women.¹³ Further, public health funding has declined over this time. Given the importance of the timing of HIV diagnosis for the individual and the public health, an assessment of HIV diagnosis in the current era seemed appropriate.

To determine characteristics of persons with recently diagnosed HIV infection in one area of the South we reviewed medical records to correlate the timing and location of HIV diagnosis with various socio-demographic factors.

Methods

Study design

We evaluated the medical records of all clinic patients initially presenting for care at the Duke University HIV clinic between October 2002 and August 2004. Only persons whose HIV infection had been diagnosed within 6 months of presentation to the clinic were included in this analysis. Abstracted data included age, gender, race/ethnicity, reported mode of HIV acquisition, insurance status, 5-digit zip code, site of diagnosis (inpatient vs. outpatient), presence of an opportunistic infection at diagnosis, initial CD4 T lymphocyte count, and initial HIV RNA level. Non-Caucasians were classified as racial/ethnic minorities. Consistent with the CDC and Office of Management and Budget classification, persons not residing in a metropolitan statistical area (population less than 50,000) were considered to reside in non-metropolitan locales.^{13,14,16} Age was categorized in 10-year increments. The study was approved by the Duke University Institutional Review Board.

Statistical analysis

Univariable analyses were performed on all study variables to ensure that distributional assumptions were met. Bivariable analyses were done using Pearson's chi-square test for dichotomous variables and logistic regression for continuous variables. The study had two primary outcome measures; a CD4 count < 200 cells/ μ L (diagnostic of immunologic AIDS) at the time of presentation, and an initial diagnosis of HIV infection while an inpatient. Multivariable logistic regression analyses were performed for both outcome variables. Predictor variables were identified a priori and included age, gender, race/ethnicity, insurance status, and rural residence. All statistical analyses were performed using SAS E-Guide Version 2.05 for Windows (SAS Institute, Cary, NC). Two-sided p-values at the 0.05 level were used to determine statistical significance ($\alpha = 0.05$).

Results

Data were available for 113 patients who met study inclusion criteria (Table 1). The study population was typical of the Duke University HIV clinic with small numbers of intravenous drug users (7%), and more than 25% women. Sixty-three percent of subjects were racial/ethnic minorities (87% African-American, 10% Latino), and nearly a third lived in non-metropolitan areas. Initial CD4 T lymphocyte counts were < 200 cells/ μ L in 49% of subjects and 35% were diagnosed during hospitalization.

Bivariable analyses

Older patients were significantly more likely to have an initial CD4 count < 200 cells/ μ L ($p=0.005$) (Table 2). Diagnosis of HIV infection during hospitalization was more common among older patients ($p=0.02$), females ($p<0.001$), and minorities ($p=0.02$) (Table 2).

Multivariable analyses

Older patients (AOR=1.72, 95% CI= 1.12,2.64, $p=0.01$) were more likely to be diagnosed with a CD4 count < 200 cells/ μ L (Table 2). Diagnosis of HIV infection during hospitalization was more common among older patients (AOR=1.79, 95% CI= 1.07,3.12, $p=0.03$) and females (AOR=6.74, 95% CI= 2.08,21.81, $p=0.001$) while lack of insurance was of borderline statistical significance (AOR=2.99, 95% CI=0.99,9.00, $p=0.05$) (Table 2).

Discussion

Despite efforts to increase HIV awareness, half the recently diagnosed HIV-infected patients evaluated at a university-based HIV clinic in North Carolina had initial CD4 T lymphocyte counts < 200 cells/ μ L compared to only 12% of those reported a decade earlier from South Carolina.¹⁵ Despite prevention and awareness campaigns, the problem of late diagnosis appears to have dramatically worsened over time. This may relate to changes in socio-demographic characteristics among persons living with HIV/AIDS, such that persons now at greatest risk are less likely to be tested due to issues of stigma and lower perceived risk. The ready availability of effective antiretroviral medications may also play a role by providing a sense of security to at risk populations thereby reducing the urgency with which they seek HIV testing. Further, declines in public health spending over this time may also contribute to this finding.

In addition to detrimental effects for the individual,⁵⁻⁷ late diagnosis of HIV infection increases risk of transmission to others. Prevention counseling that can reduce risk behaviors and secondary infections is generally focused on persons in whom HIV infection is already known.^{8,9} Therefore, patients diagnosed late have "missed out" on prevention programs for months to years while unaware of their infection. Moreover, antiretroviral therapy that

reduces HIV RNA levels almost certainly reduces risk of transmission to sexual partners.¹⁷ The delay in initiating antiretroviral therapy due to late diagnosis thus likely generates more secondary HIV infections.

Testing based on perceived risk of HIV infection, rather than broader screening approaches, likely contributes to the problem. This study shows that older patients are more likely to be diagnosed both during hospitalization and with a CD4 count < 200 cells/ μ L. Additionally, women had a 6-fold increased likelihood of being diagnosed in the hospital. This suggests that older patients and women may have lower perceived risk for HIV infection by both themselves and by their providers, and are therefore less likely to be tested for HIV as outpatients. In multivariable logistic regression analysis, uninsured patients were also more likely to be diagnosed as inpatients, perhaps because uninsured patients have less access to non-emergent health care. Living in a non-metropolitan area, a characteristic of the HIV epidemic unique to the South, was surprisingly not associated with late diagnosis of HIV infection despite the reduced availability of medical services, and increased HIV stigma in rural communities.

As a single center study our findings may not be generalizable to other medical settings or regions of the country. It is also possible that advanced HIV-infected patients may be over-represented in this sample since sicker patients may be more likely to be referred to an academic medical center for care. However, our findings are consistent with other recently reported estimates, including a cohort of patients in a large health maintenance organization.^{10,11} Given the relatively modest sample size it is possible that there was insufficient power to identify other important associations such as whether minorities and uninsured patients may be more likely diagnosed during hospitalization. Finally, as an observational study these data identify associations, but can not attribute causality.

These findings support the notion that late diagnosis of HIV infection remains a significant problem, particularly among older patients. Additionally, these data indicate diagnosis of HIV infection during hospitalization is disturbingly common, especially among older patients and women. Recent initiatives call for HIV testing to become a more routine part of medical care,^{18,19} in part because of the problem of late HIV diagnosis substantiated by this study. Routine rather than risk-based HIV testing is advocated since high-risk behaviors are frequently not identified in primary care encounters.¹¹ Prospective studies assessing the impact of routine screening in various medical settings are ongoing and will be important in developing an evidence-based HIV screening policy.

Clinical significance

- 49% of recently diagnosed HIV-infected patients had clinical and/or immunologic AIDS (CD4 T lymphocyte count < 200 cells/ μ L).
- Older patients were more likely to have an AIDS diagnosis at the time HIV was diagnosed.
- Older patients and women were more likely to be diagnosed with HIV during hospitalization.
- These findings support recent calls for more routine HIV testing in primary care settings.

Acknowledgments

These data were presented in part at the 3rd International AIDS Society Conference on HIV Pathogenesis and Treatment in Rio de Janeiro, Brazil July 25–28; 2005. Supported by an Agency for Healthcare Research and Quality (AHRQ) training grant (T32 HS000079) and an NIH K24 grant (NIAID 5 K24 AI001608).

References

1. Palella FJ Jr, Delaney KM, Moorman AC, et al. Declining morbidity and mortality among patients with advanced human immunodeficiency virus infection. HIV Outpatient Study Investigators. *N Engl J Med*. 1998 Mar 26; 338(13):853–860. [PubMed: 9516219]
2. Glynn, M.; Rhodes, P. Program and abstracts of the National HIV Prevention Conference. Atlanta: 2005 June. Estimated HIV Prevalence in the United States at the end of 2003. Abstract 595
3. Centers for Disease Control and Prevention. Late vs. Early Testing of HIV --- 16 Sites, United States, 2003–2003. *MMWR*. Vol. 52. Atlanta: 2003 June 27. p. 581–586.
4. Centers for Disease Control and Prevention. HIV/AIDS Surveillance Report, 2002. Atlanta: US Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Infectious Diseases, Division of HIV/AIDS; 2002. p. 1–48.
5. Egger M, May M, Chene G, et al. Prognosis of HIV-1-infected patients starting highly active antiretroviral therapy: a collaborative analysis of prospective studies. *Lancet*. 2002 Jul 13; 360(9327):119–129. [PubMed: 12126821]
6. Bozzette SA, Joyce G, McCaffrey DF, et al. Expenditures for the care of HIV-infected patients in the era of highly active antiretroviral therapy. *N Engl J Med*. 2001 Mar 15; 344(11):817–823. [PubMed: 11248159]
7. Chen RY, Westfall AO, Accort NA, et al. Distribution of health care expenditures for HIV-infected patients. *Clin Infect Dis*. 2006 Apr 1; 42:1003–1010. [PubMed: 16511767]
8. Centers for Disease Control and Prevention. Incorporating HIV Prevention into the Medical Care of Persons Living with HIV: Recommendations of the CDC, the HRSA, the NIH, and the HIV Medicine Association of the IDSA. Vol. 52. Atlanta: *MMWR*; 2003 July 18. p. 1–24.
9. Marks G, Crepaz N, Senterfitt JW, Janssen RS. Meta-analysis of high-risk sexual behavior in persons aware and unaware they are infected with HIV in the United States: implications for HIV prevention programs. *J Acquir Immune Defic Syndr*. 2005 Aug 1; 39(4):446–453. [PubMed: 16010168]
10. Dybul M, Bolan R, Condoluci D, et al. Evaluation of initial CD4+ T cell counts in individuals with newly diagnosed human immunodeficiency virus infection, by sex and race, in urban settings. *J Infect Dis*. 2002 Jun 15; 185(12):1818–1821. [PubMed: 12085332]
11. Klein D, Hurley LB, Merrill D, Quesenberry CP Jr. Review of medical encounters in the 5 years before a diagnosis of HIV-1 infection: implications for early detection. *J Acquir Immune Defic Syndr*. 2003 Feb 1; 32(2):143–152. [PubMed: 12571523]
12. Samet JH, Freedberg KA, Stein MD, et al. Trillion virion delay: time from testing positive for HIV to presentation for primary care. *Arch Intern Med*. 1998 Apr 13; 158(7):734–740. [PubMed: 9554679]
13. Centers for Disease Control and Prevention. HIV/AIDS Surveillance Report, 2003. Vol. Vol. 15. Atlanta: US Department of Health and Human Services, Centers for Disease Control and Prevention; 2004. p. 1–46.
14. Centers for Disease Control and Prevention. [Accessed on March 1, 2006] HIV/AIDS Surveillance in Urban and Nonurban Areas L206 slide series. Available at: <http://www.cdc.gov/hiv/graphics/rural-urban.htm>
15. Luby S, Jones J, Horan J. Using CD4 counts to evaluate the stages and epidemiology of HIV infection in South Carolina public clinic patients. *Am J Public Health*. 1994 Mar; 84(3):377–381. [PubMed: 7907458]
16. Office of Rural Health Policy. [Accessed October 17, 2005] List of Rural Counties and Designated Eligible Census Tracts in Metropolitan Counties. Available at: <ftp://ftp.hrsa.gov/ruralhealth/Eligibility2005.pdf>

17. Quinn TC, Wawer MJ, Sewankambo N, et al. Viral load and heterosexual transmission of human immunodeficiency virus type 1. Rakai Project Study Group. *N Engl J Med*. 2000 Mar 30; 342(13): 921–929. [PubMed: 10738050]
18. Beckwith CG, Flanigan TP, del Rio C, et al. It is time to implement routine, not risk-based, HIV testing. *Clin Infect Dis*. 2005 Apr 1; 40(7):1037–1040. [PubMed: 15824997]
19. Centers for Disease Control and Prevention. Advancing HIV Prevention: New Strategies for a Changing Epidemic. Vol. 52. Atlanta: MMWR; 2003 April 18. p. 329-332.

Table 1

Patient characteristics of 113 recently diagnosed HIV-infected subjects establishing care at the Duke University HIV Clinic.

Characteristic	Mean $\pm$ SD or Frequency (%)
Age (range 17–61 years)	36.1 $\pm$ 10
Female	31 (27.4%)
Race	
Caucasian	35 (31.0%)
Minority	71 (62.8%)
Unknown	7 (6.2%)
Reported mode of HIV acquisition	
Men who have sex with men	33 (29.2%)
Heterosexual contact	32 (28.3%)
Intravenous drug use	8 (7.1%)
Other/Unknown	40 (35.4%)
Uninsured	44 (38.9%)
Non-metropolitan	32 (28.3%)
Site of Diagnosis	
Inpatient HIV diagnosis	39 (34.5%)
Outpatient HIV diagnosis	54 (47.8%)
Unknown	20 (17.7%)
Opportunistic Infection at diagnosis*	20 (17.9%)
HIV RNA > 100,000 copies/mL	66 (58.9%)
CD4 Lymphocyte count <200 cells/μL	55 (48.7%)

* Opportunistic Infections: *Pneumocystis carinii* pneumonia (PCP) 9, Cryptococcal meningitis 5, Lymphoma 2, Cryptosporidial diarrhea 1, CNS toxoplasmosis 1, Progressive multifocal leukoencephalopathy 1, Kaposi's sarcoma 1

Table 2

Bivariable and multivariable logistic regression analyses. Variables associated with immunologic AIDS (CD4 count < 200 cells/ μ L) and inpatient HIV diagnosis among 113 recently diagnosed HIV-infected subjects establishing care at the Duke University HIV Clinic.

Characteristic	CD4 count < 200 cells/ μ L (n=113)				Inpatient HIV Diagnosis (n=93)			
	Bivariable analysis		Multivariable analysis		Bivariable analysis		Multivariable analysis	
	OR (95%CI)	p-value	OR (95%CI)	p-value	OR (95%CI)	p-value	OR (95%CI)	p-value
Age* (range 17–61 years)	1.74 (1.16,2.60)	0.005	1.72 (1.12,2.64)	0.01	1.63 (1.07,2.56)	0.02	1.79 (1.07,3.12)	0.03
Female	1.68 (0.73,3.88)	0.22	1.30 (0.51,3.35)	0.59	6.71 (2.52,17.87)	<0.001	6.74 (2.08,21.81)	0.001
Minority	1.37 (0.61,3.08)	0.45	1.56 (0.63,3.87)	0.34	3.27 (1.20,8.87)	0.02	2.63 (0.82,8.43)	0.10
Uninsured	0.94 (0.44,2.00)	0.87	1.06 (0.46,2.45)	0.89	1.71 (0.74,4.00)	0.21	2.99 (0.99,9.00)	0.05
Non-metropolitan	1.28 (0.57,2.91)	0.55	1.19 (0.49,2.87)	0.71	1.58 (0.63,3.93)	0.33	1.32 (0.44,3.99)	0.61

* Odds ratios for 10 year increase in age