Diagnosing HIV Infection in Primary Care Settings: Missed Opportunities

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Abstract

In the United States, 20% of HIV-infected persons are unaware of their diagnosis. Improved application of HIV screening recommendations in healthcare settings may facilitate diagnosis. Clinical patient data and previous healthcare visits were reviewed from medical records of newly diagnosed HIV-infected persons in Durham County, North Carolina, who initiated HIV care at Duke University Medical Center in 2008–2011. Comparisons were made to similar data from 2002–2004 using the Pearson's chi-square test and logistic regression. 101 consecutive newly diagnosed patients were identified: 67 males; 73 black, 20 white, and 8 Hispanic/Latino. Mean age was 39 years (range, 17–69), and 73 had health insurance. Median baseline CD4 count was 313 cells/ μ L (range, 4–1302), and HIV-1 viral load was 45,700 copies/mL (range, 165–10,000,000). One-third had a baseline CD4 count <50 cells/ μ L, and 15% presented with opportunistic infections. Compared to patients newly diagnosed in 2002–2004, significantly greater proportions were black and less immunocompromised in 2008–2011. Most had been seen at least once by a healthcare provider in the year prior to HIV diagnosis: 72 had ≥ 1 prior visits, and 47 had ≥ 2 visits. Among those with prior visits, 37/72 (51%) were seen in an emergency department on the first or second visit. Men were three times more likely than women to be diagnosed at their first healthcare encounter ($p=0.03$, OR=3.2). Despite CDC recommendations for widespread HIV screening in healthcare settings, HIV diagnosis remains delayed, even among those with frequent healthcare encounters. Educating providers and removing barriers to HIV screening may improve this problem.

Introduction

ADVANCES IN MEDICAL CARE and antiretroviral therapy (ART) have dramatically improved the lives of HIV-infected persons. Because almost one in five (18%) of the 1.2 million people living in the United States are unaware of their HIV infection,¹ these benefits do not accrue to all. Moreover, HIV-infected persons not receiving antiretroviral therapy are much more likely to spread the virus to others.² Many HIV-infected persons who are diagnosed are found late in the course of their disease.³ Despite recommendations by the Centers for Disease Control and Prevention (CDC)⁴ for more widespread testing and screening efforts,^{5,6} many HIV-infected patients make numerous visits to healthcare settings before being diagnosed.^{7–9}

In North Carolina, Durham County has one of the highest rates of diagnosed HIV disease cases (29.9 per 100,000).¹⁰ The Duke University Health System (DUHS), which includes a large academic medical center, two community hospitals, and multiple outpatient clinics, serves this county. The objective of

this study was to identify and characterize missed opportunities to diagnose HIV infection occurring prior to the actual diagnosis being made. These data were compared to a similar study of newly diagnosed patients in 2002–2004.¹¹ Based on an assumption that HIV diagnosis strategies had improved over time, we anticipated fewer missed opportunities, and thus higher CD4 counts among newly diagnosed patients.

Methods

This is a retrospective cohort study of Durham County residents linked to care and seen at the Duke HIV Clinic between November 2008 and November 2011. The Duke HIV Clinic currently follows >1800 active HIV-infected patients. Review of medical records of eligible patients was used to collect relevant data: patient demographics including sexual orientation, history of IV drug use (IVDU), and health insurance status (included among the insured were those with private insurance, Medicare, and Medicaid); baseline CD4 cell count and HIV-1 viral load; number and type of visits at

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DUHS facilities during the 12 months prior to diagnosis, number of HIV-related signs and symptoms present during prior visits and at time of diagnosis, date and place of HIV diagnosis, and opportunistic infections (OI) at time of diagnosis. Demographic and clinical characteristics were compared to a similar cohort of newly diagnosed patients from 2002–2004.¹¹

A missed opportunity for HIV diagnosis was defined as a prior healthcare encounter occurring in the 12 months prior to the date of initial HIV-1 ELISA test or the visit date when the confirmatory HIV test was ordered (whichever date was earlier). Prior visits included those occurring in the DUHS primary care clinics, emergency departments (ED) and urgent care centers, or in any DUHS subspecialty clinic (excluding Ophthalmology, Radiology, Surgery, Anticoagulation, Wound Care, and Orthopedics). Characteristics between newly diagnosed patients with ≥ 1 missed opportunities were compared to those with no missed opportunities. HIV-related

signs and symptoms were obtained using the World Health Organization (WHO) clinical staging guidelines (Table 1).¹² OIs were recorded using the WHO guidelines (Clinical Stage 4) and the CDC AIDS-defining conditions.^{12,13} Bivariable analyses were performed using Pearson's chi-square test for dichotomous variables and logistic regression for continuous variables.

Results

Newly Diagnosed HIV Patients in 2008–2011

Between 2008 and 2011, 101 newly diagnosed HIV-infected patients living in Durham County were linked to care and seen in the Duke HIV Clinic. The majority were male (67/101, 66%), African American (73/101, 72%), and the mean age was 39 years (range, 17–69) (Table 2). Most had

TABLE 1. WHO CLINICAL CONDITIONS OR SYMPTOMS FOR ADULTS AND ADOLESCENTS WITH CONFIRMED HIV INFECTION¹²

Clinical Stage 1
Asymptomatic
Persistent generalized lymphadenopathy
Clinical Stage 2
Moderate unexplained weight loss ($<10\%$ of presumed or measured body weight)
Recurrent respiratory tract infections (sinusitis, tonsillitis, otitis media, and pharyngitis)
Herpes zoster
Angular cheilitis
Recurrent oral ulceration
Papular pruritic eruptions
Seborrheic dermatitis
Fungal nail infections
Clinical Stage 3
Unexplained severe weight loss ($>10\%$ of presumed or measured body weight)
Unexplained chronic diarrhea for longer than 1 month
Unexplained persistent fever (above 37.6°C intermittent or constant, for longer than 1 month)
Persistent oral candidiasis
Oral hairy leukoplakia
Pulmonary tuberculosis (current)
Severe bacterial infections (such as pneumonia, empyema, pyomyositis, bone or joint infection, meningitis or bacteremia)
Acute necrotizing ulcerative stomatitis, gingivitis, or periodontitis
Unexplained anemia ($<8\text{ g/dL}$), neutropenia ($<0.5 \times 10^9$ per liter) or chronic thrombocytopenia ($<50 \times 10^9$ per liter)
Clinical Stage 4
HIV wasting syndrome
Pneumocystis pneumonia
Recurrent severe bacterial pneumonia
Chronic herpes simplex infection (orolabial, genital, or anorectal of more than 1 month's duration or visceral at any site)
Esophageal candidiasis (or candidiasis of trachea, bronchi or lungs)
Extrapulmonary tuberculosis
Kaposi's sarcoma
Cytomegalovirus infection (retinitis or infection of other organs)
Central nervous system toxoplasmosis
HIV encephalopathy
Extrapulmonary cryptococcosis including meningitis
Disseminated non-tuberculous mycobacterial infection
Progressive multifocal leukoencephalopathy
Chronic cryptosporidiosis (with diarrhea)
Chronic isosporiasis
Disseminated mycosis (coccidiomycosis or histoplasmosis)
Recurrent non-typhoidal Salmonella bacteremia
Lymphoma (cerebral or B-cell non-Hodgkin) or other solid HIV-associated tumors
Invasive cervical carcinoma
Atypical disseminated leishmaniasis
Symptomatic HIV-associated nephropathy or symptomatic HIV-associated cardiomyopathy

TABLE 2. DEMOGRAPHIC AND CLINICAL CHARACTERISTICS FOR NEWLY DIAGNOSED HIV PATIENTS IN 2002–2004 AND 2008–2011

Characteristic	2002–2004 (n=113)	2008–2011 (n=101)	p Value
Age			
Mean ± SD	36.1 ± 10	38.9 ± 12.8	0.074
Gender			
Male	82 (72.6%)	67 (66.3%)	0.323
Female	31 (27.4%)	34 (33.7%)	
Race			
Black	62 (54.6%)	73 (72.3%)	0.008
White	35 (31.0%)	20 (19.8%)	
Hispanic	7 (6.3%)	8 (7.9%)	
Unknown	7 (6.2%)	0 (0%)	
Other	2 (1.9%)	0 (0%)	
Insurance			
Uninsured	44 (38.9%)	28 (27.7%)	0.083
Insured	69 (61.1%)	73 (72.3%)	
Mode of HIV acquisition			
MSM	33 (29.2%)	24 (23.8%)	0.369
Heterosexual	32 (28.3%)	57 (56.4%)	
IVDU	8 (7.1%)	4 (4.0%)	
Other ^a /unknown	40 (35.4%)	16 (15.8%)	
Site of diagnosis			
Outpatient	54 (47.8%)	73 (72.3%)	<0.001
Inpatient	39 (34.5%)	28 (27.7%)	
Unknown	20 (17.7%)	0 (0%)	
Persons w/ OI at diagnosis	20 (17.9%) ^b	15 (14.9%) ^c	0.574
CD4 lymphocyte count			
<200 cells/ μ L	55 (48.7%)	33 (32.7%)	0.018
HIV RNA			
>100,000 copies/mL	66 (58.9%)	38 (37.6%)	0.002

^aOther: transgender, bisexual; ^bopportunistic infections: CNS toxoplasmosis ($n=1$); cryptococcal meningitis ($n=5$); cryptosporidial diarrhea ($n=1$); Kaposi's sarcoma ($n=1$); lymphoma ($n=2$); *Pneumocystis jirovecii* pneumonia ($n=9$); progressive multifocal leukoencephalopathy ($n=1$). ^cOIs: CNS toxoplasmosis ($n=1$); cryptococcal meningitis ($n=1$); esophageal candidiasis ($n=4$); *Mycobacterium avium* complex ($n=1$); *Pneumocystis jirovecii* pneumonia ($n=9$); recurrent severe bacterial infections ($n=1$).

insurance (73/101, 72%), only one-third of males were men who have sex with men (MSM) (24/67, 36%), and only 4% had a history of IVDU. The median baseline CD4 count was 313 cells/ μ L (range, 4–1,302), and median baseline HIV-1 viral load was 45,700 copies/mL (range, 165–10,000,000 with 10,000,000 as the upper limit). Thirty-three (33%) met the CDC surveillance case definition for AIDS (CD4 count <200 cells/ μ L) at the time of diagnosis.

The mean number of DUHS healthcare visits per patient in the year prior to diagnosis was 2.75 (range, 0–20). The DUHS ED/Urgent Care and primary care clinics were the most common sites of new HIV diagnosis (36/101 and 26/101, respectively) as compared to DUHS subspecialty clinics, Durham County Health Department, and non-DUHS settings. Among patients diagnosed in non-DUHS settings, 17/25 (68%) were diagnosed in a primary care setting.

In the 12 months prior to their HIV diagnosis, 72/101 patients (71%) had one or more prior healthcare encounters. Among the 51 patients with available data on symptoms at prior visits, 18 (35%) had complained of HIV-associated signs

and symptoms at least once during the two visits most proximate to their HIV diagnosis. The three most common signs/symptoms included recurrent respiratory tract infections (6/18), unexplained persistent fever (4/18), and persistent generalized lymphadenopathy (4/18). Overall, 34/101 (34%) presented with HIV-associated signs/symptoms at diagnosis, and 15/34 (44%) of those with HIV signs/symptoms presented with OIs. The most common OIs were *Pneumocystis jirovecii* pneumonia (9/15) and esophageal candidiasis (4/15). Among the newly diagnosed HIV-infected with opportunistic infections, 12/15 (80%) had been seen by a healthcare provider at least once in the year prior to diagnosis, and the mean number of encounters with the healthcare system in the year prior for those with OIs was 2.8 (range, 0–10).

Newly diagnosed HIV patients in 2002–2004 vs. U.S. 2008–2011

Demographic and clinical characteristics were similar between the 2002–2004 and the 2011–2008 cohorts (Table 2). The majority of patients were male, although there was a greater percentage of women in the more recent cohort (27% in 2002–2004 vs. 34% in 2008–2011; $p=0.323$). There was no significant difference in mean age. However, a significantly greater proportion of newly diagnosed patients were African American in the more recent cohort (55% vs. 72%; $p=0.008$). The proportion of MSM (29% vs. 24%), including African American MSM (11% vs. 14%), and IVDU (7% vs. 4%) were comparable in both cohorts, although 35% of the older cohort had an unknown mode of HIV acquisition. No significant difference was observed in the percentage of uninsured (39% vs. 28%; $p=0.083$). The proportion with CD4 counts <200 cells/ μ L significantly decreased over time (49% in 2002–2004 vs. 33% in 2008–2011; $p=0.018$). This trend also occurred with HIV-1 viral loads of >100,000 copies/mL (59% vs. 38%; $p=0.002$).

A significantly greater proportion of patients in the more recent cohort were diagnosed in the outpatient setting (48% in 2002–2004 vs. 72% in 2008–2011; $p=0.0003$), although site of diagnosis could not be determined in 18% of the older cohort. Lymphoma (diffuse large B-cell and Hodgkin's), cryptosporidial diarrhea, progressive multifocal leukoencephalopathy, and Kaposi's sarcoma were not diagnosed as before. However, the number of cases of *Pneumocystis jirovecii* pneumonia remained the same ($n=9$).

Newly diagnosed HIV patients with no missed opportunities vs. missed opportunities for HIV screening

During the 12 months prior to HIV diagnosis, 29 patients (29%) had no DUHS healthcare visits, 25 (25%) had one encounter and 47 (47%) had two or more. A characteristic significantly associated with missed opportunities for HIV screening was being female ($p=0.027$) (Table 3). HIV-infected males were greater than three times more likely to be diagnosed at the first healthcare encounter compared to females (OR 3.24; 95% CI 1.11–9.46). Patients without insurance were almost two times more likely to be diagnosed at the first visit versus those who were insured (OR 1.98; 95% CI 0.78–4.99), and white and Hispanic patients were almost two times more likely to be diagnosed at the first encounter compared to African Americans (OR 0.51; 95% CI 0.20–1.28). There was no difference between the two groups with regard to age or mode of HIV acquisition.

TABLE 3. CHARACTERISTICS FOR NEWLY DIAGNOSED HIV PATIENTS WITH NO MISSED OPPORTUNITIES VS. MISSED OPPORTUNITIES FOR HIV DIAGNOSIS IN 2008–2011

Characteristic	0 Missed opportunities (n = 29)	≥ 1 Missed opportunities (n = 72)	p Value	OR (95% CI)
Age ^a				
Mean ± SD	36.1 ± 12.2	40.0 ± 12.7	0.17	0.97 (0.94–1.01)
Gender				
Male (n = 67)	24 (82.8%)	43 (59.7%)	0.027	3.24 (1.11–9.46)
Female (n = 34)	5 (17.2%)	29 (40.3%)		
Race				
Black (n = 73)	18 (62.1%)	55 (76.4%)	0.146	0.51 (0.20–1.28)
White (n = 20)	6 (20.7%)	14 (19.4%)		
Hispanic (n = 8)	5 (17.2%)	3 (4.2%)		
Insurance				
Uninsured (n = 28)	11 (37.9%)	17 (23.6%)	0.146	1.98 (0.78–4.99)
Insured (n = 73)	18 (62.1%)	55 (76.4%)		
Mode of HIV acquisition				
MSM (n = 24)	9 (31.0%)	15 (20.8%)	0.276	1.71 (0.65–4.51)
Heterosexual (n = 57)	12 (41.4%)	45 (62.5%)		
IVDU (n = 4)	2 (6.9%)	2 (2.8%)		
Other ^b /unknown (n = 16)	6 (20.7%)	10 (13.9%)		
Site of diagnosis				
Outpatient (n = 73)	22 (75.9%)	51 (70.8%)	0.610	1.29 (0.48–3.49)
Inpatient (n = 28)	7 (24.1%)	21 (29.2%)		
Persons w/ OI at diagnosis (n = 15)	3 (10.3%) ^c	12 (16.7%) ^d	0.419	0.58 (0.15–2.17)
CD4 lymphocyte count				
< 200 cells/μL (n = 33)	9 (31.0%)	24 (33.3%)	0.823	0.90 (0.36–2.27)
HIV RNA				
> 100,000 copies/mL (n = 38)	9 (31.0%)	29 (40.3%)	0.386	0.67 (0.27–1.67)

^aOdds ratio for 10-year increase in age; ^bother: transgender, bisexual; ^copportunistic infections: esophageal candidiasis (n = 2); *Pneumocystis jirovecii* pneumonia (n = 1). ^dOIs: CNS toxoplasmosis (n = 1); cryptococcal meningitis (n = 1); esophageal candidiasis (n = 2); *Mycobacterium avium* complex (n = 1); *Pneumocystis jirovecii* pneumonia (n = 8); recurrent severe bacterial infections (n = 1).

Baseline CD4 counts and HIV-1 viral loads were not different in those diagnosed at the first encounter compared to those with missed opportunities. The number and variety of OIs were much greater among patients with missed opportunities (3 OIs in patients with no missed opportunities vs. 12 in patients with ≥ 1 missed opportunities) and included: disseminated *Mycobacterium avium* complex (n = 1), cryptococcal meningitis (n = 1), CNS toxoplasmosis (n = 1), recurrent severe bacterial infections (n = 1), in addition to *Pneumocystis jirovecii* pneumonia (n = 8).

Among the 72 patients with ≥ 1 missed opportunities, 37 (51%) patients had ≥ 1 visit to the ED, 10 (14%) had ≥ 1 visit to an Urgent Care facility, 24 (33%) had ≥ 1 visit to a primary care clinic other than the ED/Urgent Care, and 1 (1%) had been hospitalized in their two most recent healthcare encounters. Among the 47 patients with ≥ 2 missed opportunities, 25 (53%) were seen in an ED and 22 (47%) in a primary care clinic in at least one of the two most recent pre-diagnosis encounters. The most common sites of diagnosis among patients with no missed opportunities were non-DUHS settings (12/29, 41%) and the ED (11/29, 38%). Out of those with diagnoses at non-DUHS settings, 9/12 (75%) were diagnosed in a primary care setting. For those with missed opportunities, the ED was the most common site of diagnosis (23/72, 32%), followed by DUHS primary care clinics (22/72, 31%). Out of 13 with missed opportunities and diagnoses at non-DUHS settings, 8/13 (62%) were diagnosed in a primary care setting.

Discussion

One of the most important factors in the ongoing epidemic of HIV infection is transmission from persons unaware of being HIV infected. In an effort to combat this vexing problem, the CDC published new guidelines for HIV testing in 2006 that were designed to simplify the process and make testing universal in all healthcare settings.⁴ Our data on newly diagnosed patients collected before and after the CDC testing guidelines suggest there has been variable impact in healthcare settings where the greatest opportunity to diagnose HIV infection exists—ED's and primary care settings.

Although persons with newly diagnosed HIV infection in 2008–2011 had meaningfully higher CD4 counts compared to persons in 2002–2004, suggesting earlier diagnosis, they also had a mean of 2.75 visits in the year prior to diagnosis indicating ongoing missed opportunities. Discouragingly, being female was associated with missed diagnostic opportunities, which likely reflects an ongoing stereotype as to at-risk profiles, an issue the 2006 guidelines were intended to diminish in importance.

In our cohort, the racial preponderance has evolved; just over half (55%) were African American in 2002–2004, with an increase to 72% in 2008–2011. This finding may reflect the changing demographics of HIV in the U.S., particularly in the Southeast, where 72% of our overall HIV clinic population is African American. Although African American MSM represent

an increasing percentage of HIV infected persons in the U.S.,¹⁴ we did not see a similar significant trend among this population but rather an increase in heterosexuals newly diagnosed between 2002–2004 vs. 2008–2011, though this may be driven by an increase in females.

The ED represented the most common site for diagnosis in our recent cohort in addition to being the most common site for missed opportunities. Nationally, EDs have already been recognized as valuable settings for large volume HIV screening.^{15,16} The positive prevalence rates of these programs have been modest, ranging from 0.14% to 1.7% of tested persons.¹⁷ Of note, the DUHS ED has had an ongoing, free, nontargeted, voluntary HIV screening program since 2008. Six of the 101 newly diagnosed patients (6%) in the 2008–2011 cohort were diagnosed by way of this ED screening program. Overall, 7 new diagnoses have been made through the ED screening program, and 6/7 (86%) have been successfully linked to care.¹⁸

In the present study, females were significantly more likely to have ≥ 1 missed opportunities for HIV diagnosis, not described in other studies. This finding may in part be due to ongoing stereotypes and/or to women's higher utilization of health services compared to men, and thus, a greater chance of missed opportunities, though visits for prenatal HIV and cervical cancer screenings make HIV screening more widely accessible to women.

This study may be limited in generalizability to other medical settings and regions, given its focus on one county in the Southeast. Nonetheless, southeastern U.S. is the area with the highest new HIV infection rate,¹⁹ and as such, this study is likely applicable to a substantial proportion of the current HIV epidemic.

Despite the 2006 CDC recommendations for universal HIV screening in all healthcare settings,⁴ this research confirms that opportunities to diagnose HIV infection in persons seeking healthcare are often missed, even among those with frequent healthcare interactions, and particularly among women. A more systematic approach to HIV screening in the ED and primary care settings may improve overall diagnosis since they were the sites with the most missed encounters as well as the sites for the highest number of HIV diagnoses. Education of providers combined with improved access to HIV screening tools may provide significant dividends.

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Author Disclosure Statement

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