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Risk factors for AIDS-defining illnesses among a cohort of poorly adherent people living with HIV/AIDS in Atlanta, Georgia

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Abstract

In order to achieve the programmatic goals established in the National HIV/AIDS Strategy, virologic suppression remains the most important outcome within the HIV care continuum for individuals receiving antiretroviral therapy (ART). Therefore, clinicians have dedicated substantial resources to improve adherence and clinic retention for individuals on ART; however, these efforts should be focused first on those most at risk of morbidity and mortality related to AIDS. Our study aimed to characterize the factors that are associated with AIDS-defining illnesses (ADIs) amongst people living with HIV (PLHIV) who are poorly adherent or retained in care in order to identify those at highest risk for poor clinical outcomes. We recruited 99 adult PLHIV with a history of poor adherence to ART, poor clinic attendance, or unsuppressed viral load from the Infectious Disease Program (IDP) of the Grady Health System in Atlanta, GA between January and May of 2011 to participate in a survey investigating the acceptability of a financial incentive for improving adherence. Clinical outcomes including the number of ADI episodes in the last five

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years, viral loads, and CD4 counts were abstracted from medical records. Associations between survey items and number of ADIs were performed using Chi-square analysis. In our study, 36.4% of participants had ≥1 ADI in the last five years. The most common ADIs were *Pneumocystis jirovecii* pneumonia, recurrent bacterial pneumonia, and esophageal candidiasis. Age <42.5 years (OR 2.52, 95%CI 1.08-5.86), Male gender (OR 3.51, 95%CI 1.08-11.34), CD4 nadir <200 cells/μL (OR 11.92, 95%CI 1.51-94.15), unemployment (OR 3.54, 95%CI 1.20-10.40), and travel time to clinic <30 minutes (OR 2.80, 95%CI 1.20-6.52) were all significantly associated with a history of ≥1 ADI in the last five years. Awareness of factors associated with ADIs may help clinicians identify which poorly adherent PLHIV are at highest risk for HIV-related morbidity.

Keywords

AIDS-defining illness; opportunistic infection; HIV adherence

Introduction

Despite the availability of antiretroviral therapy (ART) for HIV infection, achieving virologic suppression remains a significant challenge for many people living with HIV (PLHIV). Virologic suppression depends on two components: clinic attendance and ART adherence. Several studies have identified barriers to ART adherence including alcohol consumption, employment outside the home(Chesney et al., 2000), medication availability, forgetfulness, and being busy with other things(Amico et al., 2007; Chesney et al., 2000). On the other hand, barriers to clinic retention have been more difficult to define because they tend to be more diverse and regionally dependent. However, retention in care is just as vital as medication adherence, as missed appointments have been shown to predict HIV progression(Berg et al., 2005; Park et al., 2007; Rastegar, Fingerhood, & Jasinski, 2003) and increased mortality(Giordano et al., 2007; Mugavero et al., 2009). Despite many reasons for poor adherence to ART or clinical care, little is known about which of these patients will have poor clinical outcomes. In this study, we aimed to identify risk factors that are associated with AIDS-defining illnesses (ADIs) in poorly adherent PLHIV.

Methods

Patients

Ninety-nine adult (≥18 years old) PLHIV were recruited from the Infectious Disease Program (IDP) of the Grady Health System in Atlanta, GA between January and May of 2011. The IDP is an outpatient clinic that served approximately 5,200 PLHIV (46.72% uninsured, 25.78% Medicaid, and 22.84% Medicare) in 2011 who had a diagnosis of AIDS. Participants were identified by chart review and referred from clinic providers in two phases. The first phase enrolled patients with a clinic visit within the last 1.5 years but not within the prior six months, and who had a history of poor ART adherence and/or a most recent HIV-1 viral load (VL) > 200 copies/ml. In the second phase, recent clinic attendance was not an exclusion criteria, but the most recent VL had to be > 200 copies/mL after ≥6 months of ART. All participants could not be actively abusing illicit substances since the survey was designed to determine the feasibility of a financial incentive.

Survey methods

Data was obtained from a survey investigating the acceptability of a financial incentive for improving adherence among poorly adherent PLHIV (Clinical Trials # NCT01305590). The survey was conducted using a semi-structured interview by trained interviewers in a private setting and included questions regarding medication adherence, attitudes toward proposed interventions for improving adherence, demographics, transportation, and employment. Participants provided written informed consent and were compensated for their time. All study procedures and instruments were approved by the Institutional Review Board at Emory University.

Definitions and statistical analysis

Study variables included age, gender, actively taking prescribed ART at the time of survey (as documented by providers in medical chart), employment, travel time to clinic, and mode of transportation. Participants were divided into two groups based on the mean age (42.5 years). The most recent CD4 counts (≤9) were abstracted up to five years prior to enrollment and CD4 nadir was defined as the lowest abstracted CD4 count. Travel time to clinic was stratified into < and ≥ 30 minutes. Participants were grouped into two categories based on mode of transportation: public transport and walking; and car, motorcycle, and other. Car and motorcycle were combined because these participants were thought to have greater control over their transportation, compared with those who took public transportation or walk to clinic.

Medical charts were abstracted for each unique ADI event as defined by the CDC(Schneider et al., 2008) from the preceding five years. ADIs were validated by reviewing diagnostic studies and cultures if available, but diagnoses were otherwise assumed if listed in the medical record. Participants were stratified based on the presence or absence of ADIs.

Chi-square analyses were performed to determine the associations between study variables and history of ADI using bivariate analyses. All data analyses were performed using SPSS version 22.

Results

Characteristics of study population

The study participants were predominantly male and African-American; mean age was 42.5 years (Table 1). The median CD4 count at enrollment was 154 cells/μL, the median CD4 nadir was 79 cells/μL, 56% were taking ART according to provider documentation, and 30.7% had virologic suppression at study enrollment. Participants had HIV for a median of 11.1 years. Sixty-nine percent were unemployed. 42.4% traveled <30 minutes to clinic, and 53.5% walked or took public transport to clinic.

AIDS-defining illnesses

In the last five years, 25.3% had 1-2 ADIs, and 11.1% had 3 or more. The most common ADIs were *Pneumocystis jirovecii* pneumonia (24 events), recurrent bacterial pneumonia (23 events), and esophageal candidiasis (14 events) (Table 2). Age <42.5 years (OR 2.52,

95%CI=1.08-5.86)), Male gender (OR 3.51, 95%CI=1.08-11.34)), CD4 nadir <200 cells/μL (OR 11.92, 95%CI=1.51-94.15), unemployment (OR 3.54, 95%CI=1.20-10.40), and travel time to clinic <30 minutes (OR 2.8, 95%CI=1.20-6.52) were all significantly associated with a history of ≥1 ADI in the last five years (Table 3). No association was found between current ART usage and mode of transport with the presence of ADIs.

Discussion

Overall, the participants were mostly male, African-American, middle aged, unemployed, and had been diagnosed with HIV for more than a decade. The participants traveled variable amounts of time to clinic, which is at least partly explained by the clinic's wide catchment area, which includes 20 counties in the eligible Atlanta metropolitan area. The low mean CD4 count and nadir, low percentage who achieved virologic suppression, and low percentage taking ART, in conjunction with the long duration of time since diagnosis confirm that this is a group with poor adherence.

In our study, age <42.5 years was significantly associated with a history of ≥1 ADI in the last five years. Prior studies have suggested that older age (>50 years old) reduced the risk of non-adherence(Ghidei et al., 2013; Weintrob et al., 2008), and that younger patients had a higher risk of poor retention in care(Hall et al., 2013). By extension, older individuals would likely have lower risk of ADIs despite studies showing poorer immune reconstitution and immunosenescence(Pirrone et al., 2013).

We also found that male gender was significantly associated with a history of ADI. Previous large US studies have shown that the incidence of opportunistic infections in women has been higher than men (Buchacz et al., 2010). However, our study participants were predominantly African American, while the aforementioned study included mostly non-Hispanic Whites. In our study, the average CD4 count at enrollment was 198 cells/μL for males and 270 cells/μL for females (p=0.151). Despite the non-significant p-value, the mean enrollment CD4 count in males was below 200 cells/μL, the clinical cutoff for AIDS, which may also explain the increased risk for ADI among males in our study.

Moreover, a CD4 nadir <200 cells/μL was associated with a history of ≥1 ADIs and had the highest odds ratio (11.92) of any of the factors, confirming the known biological relationship between low CD4 count and ADIs. Of note, few participants had a CD4 nadir ≥200 cells/μL, reflecting the enrollment criteria of the IDP clinic, which requires a history of a diagnosis of AIDS.

Unemployment was also found to be linked to a history of ADI in the last five years. While this association may seem intuitive, different studies have shown mixed effects of employment on HIV outcomes. One study identified employment as a predictor of CD4 count improvement after ART initiation(Simoni, Yard, & Huh, 2013). Conversely, another showed an association between employment outside the home and poorer adherence to ART, though its effect on ADI or CD4 count was not described(Chesney et al., 2000).

Transportation has also been described as a barrier to receiving HIV care by patients(Kempf et al., 2010) and providers in the Southeast US(Reif, Golin, & Smith, 2005). In our study, a

travel time to clinic <30 minutes but not the mode of transportation was associated with a history of ADI. This apparent paradox may be due to the clinic's urban setting and may be confounded by secondary factors associated with urban living such as drug abuse(Ohl et al., 2010), homelessness(Milloy, Marshall, Montaner, & Wood, 2012), and poverty(Shacham, Lian, Onen, Donovan, & Overton, 2013).

One of the limitations of the study is the cross-sectional design, which prevents the determination of causality. In addition, there may be an element of prevalence-incidence bias since patients who may have died of ADIs could not be included in the study. The study also only includes PLHIV in Atlanta, and the results may not be generalizable to all regions. Finally, the study excluded participants with active drug abuse, so conclusions cannot be generalized to this group.

In conclusion, our data show that there is still substantial HIV-related morbidity among PLHIV in the Southeast US, and many challenges remain in achieving widespread virologic suppression. Our study has identified certain factors—young age, male gender, CD4 nadir <200 cells/μL, unemployment, and travel time <30 minutes—that are associated with ADI in poorly adherent PLHIV. Awareness of these factors may help direct further studies to decrease the risk for ADI in this region where a significant burden of HIV remains.

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Table 1

Characteristics of poorly adherent PLHIV, Infectious Diseases Program, Atlanta, GA, 2011, *N*=99

	Overall	Phase 1 *n*=52	Phase 2 *n*=47
Mean age at enrollment (years)	42.5	43.4	41.5
Gender:			
Male	76%	65.4%	88.6%
Female	24%	34.6%	11.4%
Race:			
African American	85.9%	84.6%	87.2%
Other	14.1%	15.4%	12.8%
Median CD4 at enrollment, cells/μL (Q1,Q3)*	154 (94,277)	171.5 (90.3,334.8)	146 (97,247)
Median CD4 nadir in last 5 years, cells/μL(Ql,Q3)*	79 (19,154)	98.5 (19.3,192.8)	56 (17,105)
Taking antiretroviral therapy at enrollment**	56.6%	50%	63.8%
Virologic suppression (VL>200 copies/mL) at enrollment	30.7%	38.5%	23.4%
Median years since diagnosis (Q1,Q3)*	11.1 (6.1,15.8)	10.9 (6.7,15.8)	12.5 (4.3,15.8)
Employment:			
Employed	31%	26%	31.9%
Unemployed	69%	74%	68.1%
Travel time to clinic:			
<30 minutes	42.4%	32.7%	53.2%
≥30 minutes	57.6%	67.3%	46.8%
Mode of transport to clinic:			
Walking or public transport	53.5%	65.4%	40.4%
Car, motorcycle, other	46.5%	34.6%	59.6%
Number of AIDS-defining illnesses in last 5 years			
0	63.6%	69.2%	57.4%
≥1	36.4%	30.8%	42.6%

* Q1, Q3: First and third quartile

** as documented by HIV provider in medical chart

Table 2
Frequency of AIDS-defining illnesses among study participants

AIDS-defining illness	# of Unique Events
Pneumocystis jirovecii pneumonia	24
Pneumonia, recurrent	23
Candidiasis of esophagus	14
Herpes simplex, chronic ulcers (>1 month's duration) or bronchitis, pneumonitis, or esophagitis	11
Encephalopathy, HIV-related	4
Cytomegalovirus disease	3
HIV wasting syndrome	3
Ciyptococcosis, extrapulmonary	2
Cryptosporidiosis	1
Kaposi sarcoma	1
Mycobacterium tuberculosis	1
Progressive multifocal encephalopathy	1
Toxoplasmosis of brain	1

Table 3

Factors associated with a history of AIDS-defining illnesses (ADIs) in the last live years, *N*=99

	0 ADI Participants, *n* (%)	≥ 1 ADI Participants, *n* (%)	Odds Ratio (95% CI)
Age at enrollment:			
<42.5 years	26 (53.1%)	23 (46.9%)	2.52***
≥42.5 years	37 (74.0%)	13 (26.0%)	(1.08-5.86)
Gender*:			
Male	42 (57.5%)	31 (42.5%)	3.51***
Female	19 (82.6%)	4 (17.4%)	(1.08-11.34)
CD4 nadir			
<200 cells/μL	47 (57.3%)	35 (42.7%)	11.92***
≥200 cells/μL	16 (94.1%)	1 (5.9%)	(1.51-94.15)
Taking antiretroviral therapy at enrollment:			
No	29 (67.4%)	14 (32.6%)	0.75
Yes	34 (60.7%)	22 (39.3%)	(0.32-1.72)
Employment**:			
Unemployed	39 (56.5%)	30 (43.5%)	354***
Employed	23 (82.1%)	5 (17.9%)	(1.20-10.40)
Travel time to clinic			
<30 minutes	21 (50.0%)	21 (50.0%)	2.80***
≥30 minutes	42 (73.7%)	15 (26.3%)	(1.20-6.52)
Mode of transport to clinic:			
Public transport or walking	37 (69.8%)	16 (30.2%)	0.56
Car, motorcycle other	26 (56.5%)	20 (43.5%)	(0.25-1.29)

* 3 transgender participants excluded from analysis

** 2 participants who omitted question excluded from analysis

*** Chi-square $p<0.05$