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Food Insufficiency is a Risk Factor for Suboptimal Antiretroviral Therapy Adherence among HIV-Infected Adults in Urban Peru

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Abstract

We examined the relationship between food insufficiency and antiretroviral therapy (ART) adherence. A cohort of HIV-infected adults in urban Peru was followed for a two-year period after ART initiation. ART adherence was measured using a 30-day self-report tool and classified as suboptimal if <95% adherence was reported. We conducted a repeated measures cohort analysis to examine whether food insufficiency was more common during months of suboptimal adherence relative to months with optimal adherence. 1,264 adherence interviews were conducted for 134 individuals. Participants who reported food insufficiency in the month prior to interview were more likely to experience suboptimal adherence than those who did not (odds ratio [O.R.]:2.4; 95% confidence interval [C.I.]:1.4, 4.1), even after adjusting for baseline social support score (O.R. per 5 point increase:0.91; C.I.:[0.85, 0.98]) and good baseline adherence self-efficacy (O.R.: 0.25; C.I.:[0.09, 0.69]). Interventions that ensure food security for HIV-infected individuals may help sustain high levels of adherence.

Keywords

HIV/AIDS; antiretroviral therapy; adherence; food insecurity; poverty

INTRODUCTION

Household food insecurity exists when there is uncertain, insufficient or unacceptable availability, access or utilization of food. Food insufficiency is one aspect of the construct of food insecurity and refers to periods of time when individuals or households have involuntarily experienced reductions in dietary intake because of lack of social or economic resources [1]. Both food insecurity and Human Immunodeficiency Virus (HIV) disproportionately affect individuals living in areas of poverty, and existing evidence suggests a complex relationship between these two conditions. Food insecurity may increase the risk of HIV acquisition through high risk sexual behavior in exchange for money or food [2], and both food insecurity and malnutrition have been shown to predict unfavorable treatment outcomes among HIV-infected individuals [3-7]. HIV-infection may also increase the risk of food insecurity. Individuals infected with HIV demonstrate greater energy requirements compared to uninfected individuals [8]; however, loss of employment or

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productivity due to HIV-related illness [9-11] and higher medical costs may intensify food insecurity at a time when adequate nutrition is critical. Given the circular relationship between food insecurity and HIV-infection, it is not surprising that food insecurity and food insufficiency have been observed among HIV-infected populations [3, 12, 13].

Highly active antiretroviral therapy (ART) prolongs survival and reduces HIV-related morbidity [14-16]. Individuals who sustain adequate levels of adherence experience better treatment outcomes than those who do not [17,18]. Maintaining high levels of ART adherence is challenging, however, and economic barriers – such as inability to pay for transportation to the clinic, user fees, and payment for ART or associated medical tests – may contribute to suboptimal adherence [19-23]. Multiple qualitative and descriptive studies point to a causal relationship between hunger or lack of food and reduced ART adherence [19, 24-27]; however, quantitative evidence to support this hypothesis is limited. In San Francisco, Weiser and colleagues found that individuals who met the definition for severely food insecure were more likely to have ≤ 80% ART adherence [3]. Other indirect quantitative evidence comes from a pilot study conducted in Zambia, which found that individuals with food insecurity who received nutritional support demonstrated significantly better ART pill pick-up attendance compared to a group who did not receive this support [28]. To further study the association between food insufficiency and suboptimal ART adherence, we investigated this relationship in a cohort of HIV-infected adults living in poverty in Lima, Peru.

METHODS

Study population

The study population consisted of HIV-infected adults who met World Health Organization criteria for ART initiation and enrolled in a prospective study designed to evaluate the effectiveness of a community-based ART adherence intervention, which included daily social support and modified directly observed treatment (DOT). Participants in the intervention arm also received comprehensive support, including financial aid for diagnostic tests and medications to treat opportunistic infections and adverse events, and transportation and nutritional support, as needed. A description of the intervention and study results have been published [4]. The ART adherence intervention was made available to patients living in a single health region, with priority given to women and individuals with tuberculosis disease. Patients in a neighboring health area who could be matched to intervention cases by age, risk group, and/or baseline CD4 cell count, comprised the comparison group. Study enrollment took place from December 2005 to April 2007, and each participant was followed for two years or until death or loss-to-follow-up, whichever came first. Because we began routine food insufficiency measurement beginning in August 2006, only interviews conducted after this time were included in this analysis. We excluded individuals who enrolled in the intervention study but did not initiate ART or lacked at least one adherence interview.

Exposure and outcome data

To collect data on ART adherence and food insufficiency, study workers conducted home-based interviews. For intervention participants, interviews took place monthly until June 2007 and every three months thereafter throughout the two-year follow-up period. Participants in the comparison arm completed interviews every three months throughout the follow-up period. We measured ART adherence using a 30-day self-report tool that we adapted from the Adult AIDS Clinical Trials Groups (AACTG) self-report tool [29]. ART adherence self-reports have been shown to correlate with other indirect measures of adherence and have demonstrated statistically significant associations with virologic and

immunologic outcomes [30, 31]. We defined a suboptimal ART adherence month as any month for which the patient reported taking < 95% of prescribed ART pills. Doses that were missed due to clinician-initiated suspension of medications did not count towards the definition of suboptimal adherence. Because self-reported adherence levels < 95% were uncommon, we also conducted an analysis in which we defined suboptimal adherence as < 100% of prescribed ART pills.

To assess food insufficiency, patients were asked to recall the frequency with which there was not enough food for his/her household in the month prior to interview: never, sometimes, often or almost always. A similar single-question assessment of food insufficiency has been validated in a U.S. population [32]. We elected this measure because it could serve as a practical screening tool in a clinical setting. The following baseline variables were collected during baseline interviews or clinical chart review: age, sex, had spouse or partner, education level, employment status, lack of basic services (running water, electricity or plumbing), substance use, current tuberculosis disease, history of not eating for at least one day in the three months prior to study enrollment due to poverty (henceforth, baseline food insufficiency), CD4 cell count and psychosocial measures including perceived HIV-related stigma (Berger HIV Stigma Scale) [33], depression (Hopkins Symptom Checklist-15) [34,35], social support (Duke-UNC Functional Social Support Questionnaire) [36] quality of life (Medical Outcomes Study HIV Health Survey) [37,38] and HIV self-efficacy (each participant was asked whether s/he thought s/he could adhere to ART).

Statistical analyses

For all analyses we examined food insufficiency in the month prior to interview as a binary variable (any versus none) and as a categorical variable, which was tested for linearity using a likelihood ratio test with two degrees of freedom. Perceived stigma, social support and quality of life were treated as continuous linear variables, and depression was dichotomized at a mean per-item score of 1.75 [39]. We conducted a traditional cohort analysis, which consisted of repeated measures regression analyses using generalized linear models with a binomial distribution, logit link function, and compound symmetry correlation structure. We forced variables for food insufficiency, study arm and time since ART initiation into the final model and used stepwise splines to model days on treatment [40]. The final multivariable model also included all other baseline socio-demographic, clinical and psychosocial variables that predicted suboptimal adherence at a significance level of p-value < 0.20 in univariable analysis and < 0.05 in multivariable analyses as well as baseline variables that changed the effect estimate for food insufficiency by greater than 10% in either direction. We examined whether any relationship between food insufficiency and suboptimal adherence was modified by study arm. All statistical procedures were conducted in SAS Version 9.1.

RESULTS

Of the 134 HIV-infected adults included in these analyses, more than half were female (59.0%) and the mean age was 32 years (standard deviation: 7.7, Table 1). Twenty-one women (26.6% of all women) were pregnant at baseline. Participants demonstrated a high degree of socioeconomic vulnerability: 22.4% lacked access to at least one basic service (electricity, water, and/or plumbing) in their home, and 48.1% reported baseline food insufficiency.

A total of 1,279 interviews were conducted for the study cohort after the introduction of food insufficiency questions (median per person: 9, interquartile range [IQR]: 6 - 13), and 15 (1.2%) of these interviews were excluded due to a lack of dosing data (N=3) or food insufficiency data (N=12). Overall, participants self-reported high levels of ART adherence

in the 1,264 interviews included for analysis. At least one missed dose was reported in 47 (3.7%) of the 30-day recall interviews and a total of 36 (26.9%) individuals reported at least one missed dose during any 30-day recall interview during the follow-up period. During months in which at least one dose was missed the median percentage of doses missed was 3.3% (IQR: 1.7– 10.0%). We observed variability in the percentage of interview months in which study participants experienced food insufficiency (median: 41.7% of interview months; IQR: 22.2% – 66.7%). Individuals with baseline food insufficiency reported food insufficiency in a greater percentage of adherence interviews compared to those without this baseline history (median percentage: 51.4% versus 39.0%, respectively; Wilcoxon rank sum p-value (p)=0.004).

In a univariable analysis, any household food insufficiency was associated with a two-fold increase in the odds of suboptimal ART adherence (odds ratio (O.R.): 2.2; 95% Confidence Interval (C.I.): 1.3–3.8; Z-statistic (Z)=2.97; p=0.003; Table 2). None of the potential confounders displayed in Table 1 changed the effect estimate by greater than 10% in either direction; however, good adherence self-efficacy (e.g., belief that s/he could adhere to ART) and a higher social support score at baseline were statistically significantly protective against suboptimal adherence in both univariable and multivariable analysis. The final multivariable model therefore adjusted for these two variables as well as days on ART and study arm. In multivariable analysis, any food insufficiency remained a statistically significant predictor of suboptimal ART adherence, (O.R.: 2.4; 95% C.I.: 1.4 – 4.1; Z=3.07; p=0.002; Table 2). The frequency of food insufficiency (never, sometimes, often, almost always) also demonstrated a positive linear relationship with suboptimal adherence adjusting for the same covariates (O.R. for each increase in frequency category: 1.4; 95% C.I. 1.1 – 1.8; Z=3.11; p=0.002; results not shown). The relationship between food insufficiency and suboptimal adherence was not modified by study arm (wald p-value for interaction=0.67). Results for the analysis in which we defined suboptimal adherence as < 100% of prescribed pills were similar and are shown in the Appendix.

DISCUSSION

The United Nations Millennium Development Goal to “Eradicate extreme poverty and hunger” [41] and multiple reports that call for nutritional support for HIV-infected individuals [42-44] signify a growing commitment by the global community to alleviate food insecurity and improve nutrition. In practice; however, programmatic uptake of nutritional support and other programs to ensure food security among HIV-infected individuals has been slow. This study provides quantitative evidence to support a relationship between food insufficiency and suboptimal ART adherence in a cohort of adults with high overall adherence levels. We also found that food insufficiency, which was reported by participants in a median of 42% of their interviews, was a continual problem in this population. ART delivery strategies that incorporate food insufficiency interventions may contribute to higher rates of ART adherence, in addition to alleviation of hunger and malnutrition. We believe these findings are generalizeable to other populations of HIV-infected adults that are living in poverty.

Food insufficiency may adversely influence ART adherence in a number of ways. First, food insufficiency likely contributes to acute stress, during which time food procurement may be prioritized over all other activities, including consistent pill taking. Second, ART-related side effects may increase when taken on an empty stomach, which may lead to a reluctance to take ART pills without food [24]. Third, as health improves in the weeks and months following ART initiation, hunger may increase and this may be difficult to satisfy in the presence of food insufficiency; therefore an individual may elect to skip doses to avoid ART-associated hunger [19, 25]. In an earlier report of this cohort, we found that individuals

who reported having gone a day without eating due to poverty in the three months prior to study enrollment experienced smaller odds of achieving a suppressed viral load at one year [4]. In this study, we noted that individuals who reported baseline food insufficiency were more likely to experience food insufficiency during follow-up months. The previously observed association between a baseline food insufficiency and unfavorable treatment outcomes may be at least partially explained by suboptimal ART adherence.

The large number of baseline covariates available for this cohort allowed us to rule out confounding by multiple demographic, socioeconomic, clinical, or psychosocial variables as an alternative explanation for the observed association between food insufficiency and suboptimal adherence. On the other hand we cannot exclude the possibility of confounding by other time-dependent (i.e., non-baseline) risk factors for non-adherence that were correlated food insufficiency. Another limitation is the possibility that recall bias (e.g., differential reporting of food insufficiency according to adherence level) influenced our results. If individuals who experienced a suboptimal treatment month were more likely to report food insufficiency, perhaps to justify the missed dose, this could account for the observed positive association between food insufficiency and suboptimal ART adherence; however, we found that baseline food insufficiency predicted subsequent food insufficiency. Because this baseline measurement was taken prior to any ART adherence assessment, recall bias cannot be responsible for this association. While this does exclude the possibility of recall bias for the food insufficiency variable, it does suggest that the food insufficiency variable may adequately characterize actual food insufficiency. More frequent interviews among participants in the intervention arm at the outset of the study unlikely contributed to bias in this analysis for two reasons: (1) we did not find evidence that the relationship between food insufficiency and suboptimal adherence differed by study arm; and (2) we have no reason to believe that, over all, food insufficiency and suboptimal adherence were more or less prevalent during months in which interviews were conducted relative to months in which they were not conducted. Finally, we used a single question to assess food insufficiency, which is only one aspect of food insecurity, and therefore we cannot draw conclusions about the relationship between suboptimal adherence and the broader construct of food insecurity.

CONCLUSIONS

In summary, we found that food insufficiency was positively associated with a two -fold increase in the odds of suboptimal ART adherence among HIV-infected adults in urban, Peru. We recommend food assistance for at-risk individuals as a form of adherence support. In addition, interventions aimed at improving long-term economic and social stability – such as microfinance activities, employment assistance, agricultural projects, and crisis support – should be evaluated to determine their impact on adherence and treatment outcomes. These steps are necessary for fulfillment of the Millennium Development Goals and may also play a role in the sustenance of high levels of ART adherence and good health outcomes among HIV-infected individuals.

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APPENDIX TABLE

Repeated Measures Analysis of the Relationship between Food Insufficiency and Less Than 100% Adherence to Antiretroviral Therapy (63 cases, 113 outcomes, 1,264 interview months)

	Univariable			Multivariable[a,b]		
Variable	**O.R. [95% CI]**	**Z-statistic**	**p-value**	**O.R. [95% CI]**	**Z-statistic**	**p-value**
Household food insufficiency (time-varying, any versus none)	2.0 [1.3, 3.1]	3.19	0.001	2.1 [1.4, 3.3]	3.34	0.0008
Female gender	1.6 [0.93, 2.8]	1.7	0.09			
Age (years)	0.99 [0.96, 1.02]	-0.84	0.40			
CD4 count at antiretroviral therapy start (per 20 cells/μL increase)	1.03 [0.99, 1.09]	1.35	0.18			
Active tuberculosis	0.69 [0.41, 1.1]	-1.44	0.15			
Body Mass Index (BMI) <18 (kg/m^2)	0.84 [0.43, 1.6]	-0.51	0.61			
Has spouse or partner	1.3 [0.75, 2.1]	0.87	0.39			
Low education level (primary school or illiterate)	0.96 [0.42, 2.2]	-0.08	0.93			
Unemployed	0.93 [0.52, 1.7]	-0.25	0.80			
Lacks basic services (water, electricity and/or plumbing)	1.3 [0.76, 2.0]	0.88	0.38			
Passed a day without eating due to poverty	2.0 [1.1, 3.3]	2.45	0.01			
Physician-diagnosed drug abuse/dependence	0.84 [0.29, 2.4]	-0.32	0.75			
Physician-diagnosed alcohol abuse/dependence	1.2 [0.65, 2.0]	0.48	0.63			
Depression	1.4 [0.83, 2.4]	1.27	0.20			
Good adherence self-efficacy	0.50 [0.28, 0.89]	-2.34	0.02	0.49 [0.28, 0.87]	-2.45	0.01
Social support score (per 5 point increase)	0.93 [0.88, 0.98]	-2.73	0.006	0.93 [0.88, 0.98]	-2.60	0.009
Quality of life score (per 5 point increase)	0.95 [0.85, 1.07]	-0.84	0.40			
Perceived HIV stigma score (per 5 point increase)	1.03 [0.96, 1.10]	0.72	0.47			

[a] Univariable models adjusted for day of treatment; multivariable models adjusted for day of treatment and study arm and variables shown.

[b] Analysis includes 1,261 interviews for 132 individuals with data for all covariates in model.

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Table 1

Baseline Characteristics of Study Population (n=134)[a]

Variable	n (%)
Female gender	79 (59.0)
Age (years) [b]	32.0 (7.7, 31.0)
Intervention arm	86 (64.2)
CD4 count at antiretroviral therapy start (cells/μL) [b]	133 (107, 112)
Active tuberculosis	71 (53.0)
Body Mass Index (BMI) <18 (kg/m^2) (n=130)	23 (17.7)
Has spouse or partner (n=133)	59 (44.4)
Low education level (primary school or illiterate) (n=133)	15 (11.3)
Unemployed (n=132)	92 (69.7)
Lacks basic services (water, electricity and/or plumbing)	30 (22.4)
Passed a day without eating due to poverty (n=133) [c]	64 (48.1)
Physician-diagnosed drug abuse/dependence	12 (9.0)
Physician-diagnosed alcohol abuse/dependence	34 (25.4)
Depression (n=132)	88 (66.7)
Good adherence self-efficacy (n=132) [d]	49 (37.1)
Social support score (n=132) [b]	60.4 (21.0, 63.0)
Quality of life score (n=132) [b]	39.5 (9.4, 38.5)
Perceived HIV stigma score (n=130) [b]	44.9 (16.7, 44.0)

[a] Unless otherwise noted

[b] Continuous variable, mean (S.D., median presented)

[c] Baseline food insufficiency

[d] Believes s/he can adhere to ART

Table 2

Repeated Measures Analysis of the Relationship between Food Insufficiency and Less Than 95% Adherence to Antiretroviral Therapy (36 cases, 47 outcomes, 1,264 interview months)

	Univariable			Multivariable[a,b]		
Variable	**O.R. [95% CI]**	**Z-statistic**	**p-value**	**O.R. [95% CI]**	**Z-statistic**	**p-value**
Household food insufficiency (time-varying, any versus none)	2.2 [1.3, 3.8]	2.97	0.003	2.4 [1.4, 4.1]	3.07	0.002
Female gender	2.4 [1.1, 5.1]	2.24	0.03			
Age (years)	0.97 [0.92, 1.03]	-0.91	0.36			
CD4 count at antiretroviral therapy start (per 20 cells/μL increase)	1.02 [0.97, 1.07]	0.69	0.49			
Active tuberculosis	0.65 [0.33, 1.3]	-1.25	0.21			
Body mass index (BMI) <18 (kg/m^2)	0.54 [0.19, 1.4]	-1.24	0.21			
Has spouse or partner	1.1 [0.57, 2.2]	0.36	0.72			
Low education level (primary school or illiterate)	0.69 [0.24, 1.9]	-0.71	0.48			
Unemployed	1.0 [0.48, 2.0]	-0.03	0.98			
Lacks basic services (water, electricity and/or plumbing)	1.2 [0.60, 2.4]	0.52	0.61			
Passed a day without eating due to poverty	1.3 [0.68, 2.7]	0.85	0.39			
Physician-diagnosed drug abuse/dependence	0.85 [0.18, 4.0]	-0.20	0.84			
Physician-diagnosed alcohol abuse/dependence	0.79 [0.37, 1.7]	-0.61	0.55			
Depression	1.4 [0.69, 2.9]	0.95	0.34			
Good adherence self-efficacy	0.25 [0.09, 0.68]	-2.72	0.007	0.25 [0.09, 0.69]	-2.68	0.008
Social support score (per 5 point increase)	0.91 [0.84, 0.97]	-2.64	0.008	0.91 [0.85, 0.98]	-2.51	0.01
Quality of life score (per 5 point increase)	0.96 [0.83, 1.12]	-0.52	0.60			
Perceived HIV stigma score (per 5 point increase)	1.03 [0.94, 1.12]	0.57	0.57			

[a] Univariable models adjusted for day of treatment; multivariable models adjusted for day of treatment, study arm and variables shown.

[b] Analysis includes 1,261 interviews for 132 individuals with data for all covariates in model.