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Self-Perception of Body Fat Changes and HAART Adherence in the Women's Interagency HIV Study

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Abstract

To determine the association of self-perceived fat gain or fat loss in central and peripheral body sites with adherence to highly active antiretroviral therapy (HAART) in HIV-seropositive women. 1,671 women from the Women's Interagency HIV Study who reported HAART use between April 1999 and March 2006 were studied. Adherence was defined as report of taking HAART ≥ 95% of the time during the prior 6 months. Participant report of any increase or decrease in the chest, abdomen, or upper back in the prior 6 months defined central fat gain and central fat loss, respectively. Report of any increase or decrease in the face, arms, legs or buttocks in the prior 6 months defined peripheral fat gain or peripheral fat loss. Younger age, being African-American (vs. White non-Hispanic), a history of IDU, higher HIV RNA at the previous visit, and alcohol consumption were significant predictors of HAART non-adherence ($P < 0.05$). After multivariate adjustment, self-perception of central fat gain was associated with a 1.5-fold increased odds of HAART non-adherence compared to no change. Perception of fat gain in the abdomen was the strongest predictor of HAART non-adherence when the individual body sites were studied. Women who perceive central fat gain particularly in the abdomen are at risk for decreased adherence to HAART despite recent evidence to suggest that HIV and specific antiretroviral drugs are more commonly associated with fat loss than fat gain.

Keywords

Lipodystrophy; HIV; Women; HAART adherence; body image perception

INTRODUCTION

Fat distribution changes including peripheral fat loss and central fat gain were first reported soon after the introduction of highly active antiretroviral therapy (HAART). Self-perception of these changes have been associated with lower antiretroviral therapy (ART) adherence

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(Ammassari et al. 2002; Duran et al. 2001; Santos et al. 2005). However, these studies have been limited by small numbers of observations with data collected over a short follow-up period, inadequate adjustment for confounding factors, and/or limited geographic diversity. Furthermore, few studies differentiated whether central fat gain or peripheral fat loss were more likely to be associated with changes in adherence.

Early reports of fat changes in HIV-infected women suggested that fat gain particularly central adiposity and breast enlargement might predominate in women (Dong et al. 1999; Gervasoni et al. 1999; Herry et al. 1997; Ridolfo et al. 2000). However, recent studies in women using more objective measures of fat such as MRI (Tien et al. 2006), DEXA (Mulligan et al. 2005) and anthropometry (Tien et al. 2003) show that fat loss and not fat gain appear associated with HIV.

Therefore, we examined the relationship of self-perceived fat gain and fat loss in central and peripheral body sites separately on HAART adherence using longitudinal data from the Women's Interagency HIV Study, a well characterized, ethnically diverse cohort of HIV-infected women, which is representative of HIV-infected women in the US.

METHODS

Participants and procedures

The Women's Interagency HIV Study (WIHS) is a multicenter prospective cohort study that was established in 1994 to investigate the progression of HIV in women with and at risk for HIV. A total of 3,766 women (2,791 HIV-infected and 975 HIV-uninfected) were enrolled in either 1994–1995 (n=2,623) or 2001–2002 (n=1,143) from six United States cities [New York (Bronx and Brooklyn), Chicago, Los Angeles, San Francisco and Washington DC] (Barkan et al., 1998). Every six months, participants complete a comprehensive physical examination, provide blood specimens for CD4 cell count and HIV RNA determination, and complete an interviewer-administered questionnaire, which collects data on demographics, disease characteristics, and specific ART use. At each semi-annual study visit, participants are shown photo-medication cards and are asked the names of specific ART medications used since their prior study visit. The WIHS uses a standard definition of HAART adapted from the Department of Health and Human Services/Kaiser Panel guidelines (Dybul et al. 2002; U.S. Department of Health and Human Services 2006).

Of the 2,182 HIV-seropositive women with a study visit between April 1999 and March 2006, 1,759 had used HAART at least once and had perception and adherence data at one or more semiannual visits. The first study visit where the participant reported using HAART and had perception and adherence data available is referred to as the baseline visit. Visits for which women were currently pregnant or had been pregnant at any of the four preceding visits or reported using hormones including growth hormone were excluded resulting in 88 women having no usable visits. Our final study population therefore included 1,671 women. Between April 1999 and March 2006, these 1,671 women contributed 11,132 study visits of follow-up (including the baseline visit) with a median of 6 visits (IQR: 3, 10). Data from follow-up visits were included if women were on HAART and had perception and adherence data available.

Outcome Variable

Antiretroviral adherence data were collected in the WIHS at every semiannual study visit beginning in October 1998. Participants were asked to indicate how often they had taken their antiretroviral medications as prescribed in the prior six months. Participants categorized their level of adherence into one of five categories: 100% of the time, 95–99% of the time, 75–94% of the time, <75% of the time, and have not taken any of the prescribed medications. For these

analyses, HAART adherence was dichotomized as <95% vs. ≥95% as previous adherence research has shown that HIV-RNA levels of <400 copies/ml occurred 80% of the time in patients with HAART adherence ≥ 95% (Paterson et al. 2000). The validity of this measurement has been supported by prior research in the WIHS cohort where statistically significant relationships have been found between self-reported adherence and virologic and immunologic outcomes (Wilson et al. 2002).

Exposure Variables

At each semiannual study visit beginning in April 1999, participants were asked whether they noticed any changes in the shape of their body or in the amount of fat (either loss or gain) in the chest, abdomen, face, upper back, arms, legs and buttocks. A “yes” or “no” response and an “increase”, “decrease” or “no change” response were collected for each anatomic site. The self-perception of any central fat gain or loss variables were defined as any report of fat increase or decrease in the chest, abdomen, or upper back in the last 6 months, respectively, whereas the self-perception of any peripheral fat gain or loss variables were defined as any report of fat increase or decrease in the face, arms, legs or buttocks in the last 6 months.

Other Variables

Demographic, clinical, and behavioral variables included or evaluated in multivariate models to adjust for potential confounding were: race/ethnicity (White Non-Hispanic, White Hispanic, African American Non-Hispanic, African American Hispanic, and Other), study site (Bronx, Brooklyn, Washington, DC, Los Angeles, San Francisco), education, age, alcohol consumption (abstain, <3 drinks/week, 3–13 drinks/week, >14 drinks/week), report of drug use since the last visit, history of IDU, any switch of HAART regimen since the last visit, CD4 count, and log10 HIV RNA. HIV RNA data at the visit immediately prior to the current visit was included in the analysis. When HIV RNA data from the prior visit was not available, then the HIV RNA data from 2 visits prior was used if the participant was taking HAART then. HIV RNA was measured using a nucleic acid sequence-based amplification (NASBA) technique (Organon Teknika, Durham, NC, USA) with a lower threshold of detection of 80 copies/ml.

Differences in waist and hip circumferences and weight between two consecutive visits were also calculated. Waist and hip circumferences are measured by a certified examiner at each study visit using methods adapted from the National Health and Nutrition Examination Survey (NHANES III) (CDC 1996). Except for race, the factors were all time-varying, i.e., they were updated at each visit.

DATA ANALYSES

Associations of demographic, behavioral and self-perceived and measured change in body fat with HAART non-adherence (< 95%) were estimated using logistic regression models with random effects to account for the statistical dependence among repeated measures from the same individual. This approach makes full use of within-woman changes in predictors over time, such as not perceiving fat changes for several visits and then perceiving a fat change. Odds ratios show the estimated impact of within-woman changes in covariates, which we believe better addresses the issues of interest here than marginal models such as fitted by the generalized estimating equation method (Lindsey and Lambert 1998) For presentation, we selected a model with most variables included, but without education level and CD4 count, because these had little impact on adherence or on the estimated effect of the exposure variables on adherence. Because self-perception of fat changes in specific body sites (as opposed to a composite of fat changes in central or peripheral body sites) might be associated with non-adherence, we also studied the association of perceived fat gain or fat loss in each anatomic site separately; the composite perception of body fat change in central or peripheral body sites

was replaced with a perception of body fat change in a specific body site in each of the multivariate models.

RESULTS

At the baseline visit, 24% of the women reported < 95% adherence to HAART (Table 1). The mean age was 40 years with the majority being African-American, non-drinkers and non-drug users. The median log 10 HIV RNA level was 2.6 (or 400 copies/ml). The proportion of women reporting fat gain in central and peripheral sites appeared higher than those reporting fat loss; the proportion reporting peripheral fat loss appeared higher than those reporting central fat loss. The majority of women reported no change in fat both peripherally and centrally. At baseline, more than 70% of the women who reported any history of IDU denied any central fat gain (73%) or peripheral fat loss (80%) since the last visit. The characteristics of the women at baseline appeared similar to the characteristics of the women when data from all visits were included, except for the proportion of women reporting central fat loss. When all visits were included, a similar proportion of women reported central fat loss and peripheral fat loss. Forty-two percent of the women included in the study were always adherent; 6.5% were always not adherent; and 50.9% were mixed in terms of their adherence.

Table 2 shows the association of demographic, behavioral, and body fat factors with HAART non-adherence. In the univariate analysis, younger age, being African American, report of a history of IDU, alcohol consumption regardless of light, moderate or heavy alcohol use (compared to non-drinkers), and a higher HIV viral load were associated with HAART non-adherence. These associations remained statistically significant after multivariate adjustment. Any switching of a HAART regimen was negatively associated with HAART non-adherence after multivariate adjustment.

In univariate analysis, report of any perception of central fat gain, central fat loss, and peripheral fat loss was associated with non-adherence to HAART; any perception of peripheral fat gain appeared associated, but did not reach statistical significance. After multivariate adjustment, the association of any perception of central fat gain with HAART non-adherence strengthened, whereas the association of any perception of central fat loss weakened and was of borderline statistical significance. The association of peripheral fat loss with HAART non-adherence was no longer statistically significant and its odds ratio was below 1. Changes in waist and hip circumference and body weight did not appear to be strongly associated with HAART non-adherence. There appeared to be little interaction between race/ethnicity and either report of any perceived central or peripheral fat changes on HAART non-adherence (data not shown).

When we examined the association of each individual body site separately with HAART non-adherence (Table 3), a perception of fat gain in the abdomen was strongly associated with HAART non-adherence, while perception of fat loss in the chest was associated with HAART non-adherence. Estimated effects of self-perceived gain and loss for all sites were in the direction of more non-adherence.

We also examined in a multivariable model whether self-perceived fat changes were associated with measured fat changes. We found that a change in waist size of 1 to 5 cm or > 5 cm was associated with self-perceived central fat gain [Odds ratio 1.81; 95% CI: 1.21, 2.72 and 4.67; 95% CI 2.81, 7.77, respectively]; a change in hip size of −5 to −1 cm or > −1 cm was also significantly associated with self-perceived peripheral fat loss [Odds ratios 0.36 95% CI: 0.19, 0.72 and 0.12; 95% CI: 0.06, 0.24, respectively]. The inclusion of interaction terms of race/ethnicity with measured changes did not produce strong evidence of an interaction (P>0.05).

DISCUSSION

In our large cohort of women, we found that self-perception of any central fat gain was associated with HAART non-adherence after adjusting for demographic, behavioral and objective changes in body weight and anthropometric measurements of the waist and hip. On the other hand, self-perception of any peripheral fat loss was no longer associated with HAART non-adherence, after adjustment. Consistent with the findings of another study in WIHS women, we found that light, moderate or heavy drinking, being African American, intravenous drug use, and higher HIV RNA viral load at the previous visit were associated with HAART non-adherence (Wilson et al. 2002). It is noteworthy that measured changes in circumferences of the hip and waist and in body weight appeared to have little association with non-adherence when controlled for self-perception of fat change.

Although recent studies have found that peripheral lipoatrophy and not central lipohypertrophy (which was suggested in early reports) predominate in HIV-infected women on ART, it is interesting that we found that self-perception of central fat gain was associated with HAART non-adherence. Furthermore, when we examined the association of the individual body sites with HAART non-adherence, we found that self-perception of fat gain in the abdomen was strongly associated with HAART non-adherence. Interestingly, self-perception of fat loss in the chest, more so than fat gain in the chest, was associated with HAART non-adherence. For the peripheral sites of leg and arm, any self-perception of fat change was also associated with HAART non-adherence.

While other studies have shown that body fat changes affect adherence to HAART, few studies have distinguished whether fat gain or fat loss in central sites and fat gain or fat loss in peripheral sites were more strongly associated with HAART adherence. Among 277 French patients from the APROCO cohort, Duran et al. (Duran et al. 2001) showed that the number of self-reported lipodystrophy symptoms (facial atrophy, neck or subscapular hypertrophy, breast enlargement, atrophy of upper or lower extremities or buttocks, increase in waist circumference, or phlebomegaly) were independently associated with adherence failures after adjusting for age, alcohol consumption, and poor housing conditions. Among 207 patients from the AdICoNA and LipICoNA substudies of the Italian Cohort Naïve Antiretroviral, Ammassari et al. (Ammassari et al. 2002) showed that HAART adherence decreased over time among those women who perceived any body changes (defined as fat accumulation in the abdomen, breasts, trunk, and neck, and lipomas in every body site and fat loss in the face, arms, legs and glutei). A recent cross-sectional study of 457 Brazilian adult and adolescent patients (71% men, age range 30–45 years) that examined the association of self-perception of central fat gain and peripheral fat loss separately on HAART adherence found that self-perception of peripheral fat loss was associated with HAART non-adherence after adjusting for age, gender, education, duration of stavudine use, and quality of support from family and friends. Interestingly, self-perception of central fat gain was more common among women than men and patients who used protease inhibitors from 1 to 36 months (Santos et al. 2005).

To the best of our knowledge, our study is the first to examine these relationships in a large ethnically diverse cohort of women. We found that African-American non-Hispanic women and women of other race/ethnicity are at greater risk of HAART non-adherence compared to White non-Hispanic women. Any self-perceived changes in fat or measured changes in weight, waist or hip circumferences appeared to have as much impact on non-adherence across all the race/ethnic groups. A recent study in 225 HIV-infected and 207 uninfected women of predominantly African-American or Hispanic origin in New York City addressed the issue of self-perception of body weight and found that after adjusting for BMI, lower self-perception of increased body weight was demonstrated among the African-American and Hispanic HIV-infected women who had used HAART within the last 6 months. That study however, did not

address whether the lower self-perception of increased body weight was associated with HAART adherence (Sharma et al. 2006). Any independent association of race/ethnicity with HAART non-adherence found here is a complex, multifactorial process which remains unexplained in our analyses. Possible reasons for the association between race/ethnicity and non-adherence (that could not be measured in our analysis) might be that African American women and women of other race/ethnicity may have less trust in the medical system or differences in their social situation impacting on adherence.

A limitation of our study is the use of self-reported HAART adherence data. However, a previous study in the WIHS found that self-reported HAART adherence as defined here was associated with objective measures such as CD4 count, HIV viral load and self report of sexual functioning (Wilson et al. 2002). We also could not determine whether the self-perceived body fat changes were thought to be associated with antiretroviral drug toxicity and thus led to decreased HAART adherence, or whether the body changes, particularly fat gain, were thought to be associated with restoration of health and possibly becoming more complacent about adhering to HAART. Nevertheless, an advantage of these data are that all the exposures were ascertained consistently across the cohort hence it has permitted us to examine a cumulative 'natural history' of predictors of HAART non-adherence.

In conclusion, our results suggest that self-perception of body fat changes is an important factor associated with HAART non-adherence among WIHS participants. There was little association of actual measures of change in weight or waist and hip circumference with HAART non-adherence when controlled for self-perception. Self-perception of fat gain in central body sites is associated with HAART non-adherence in spite of evidence that suggests that HIV and specific antiretroviral drugs are more commonly associated with fat loss than fat gain. Clinicians should be alert to the significance of these phenomena and be ready to explore issues of HAART adherence in those women who report the perception of gaining central fat irrespective of objective measurements.

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Table 1

Characteristics of the 1,671 HIV-seropositive women from the Women's Interagency HIV Study included in this analysis.

	At the baseline visit (n=1,671)	For all visits (n=11,132)
Non-Adherence		
Yes	401 (24%)	2718 (24%)
Age in years, mean (SD)	40 (8)	43 (8)
Race/ethnicity		
White, non-Hispanic	243 (15%)	1816 (16%)
White, Hispanic	174 (10%)	889 (8%)
African-American, non-Hispanic	896 (54%)	5890 (53%)
African-American, Hispanic	36 (2%)	250 (2%)
Other	322 (19%)	2287 (21%)
Study Site		
Bronx	329 (19.7%)	2215 (19.9%)
Brooklyn	274 (16.4%)	2137 (19.2%)
Washington, DC	242 (14.5%)	1500 (13.5%)
Los Angeles	355 (21.2%)	2163 (19.4%)
San Francisco	244 (14.6%)	1507 (13.5%)
Chicago	227 (13.6%)	1610 (14.5%)
Alcohol consumption		
Abstainer	958 (60%)	6173 (58%)
Light (< 3 drinks/week)	426 (26%)	3211 (30%)
Moderate (3–13 drinks/week)	173 (11%)	985 (9%)
Heavier (≥ 14 drinks/week)	53 (3%)	252 (2%)
Drug Use Since Last Visit		
No drugs	1229 (76%)	8411 (79%)
Marijuana only	202 (12%)	1209 (11%)
Use of heroin, cocaine, crack, methadone, or methamphetamine	186 (11%)	1013 (9%)
History of IDU	335 (25%)	2738 (28%)
Self-Perception of Central Fat		
Any gain	465 (28%)	3172 (28%)
Any loss	224 (13%)	1789 (16%)
No change	1061 (64%)	6685 (60%)
Self-Perception of Peripheral Fat		
Any gain	419 (25%)	2366 (21%)
Any loss	328 (20%)	2366 (21%)
No change	924 (55%)	6400 (58%)
log10 HIV RNA at the previous visit, median (25^{th}, 75^{th} percentiles)	2.60 (<1.90,3.84)	<1.90 (<1.90,3.44)
Any HAART Switch		
Yes	75 (16%)	1057 (20%)

Table 2

Univariate and multivariate adjusted odds ratios associated with self-reported <95% non-adherence to HAART (n=1,671)

Variable	Univariate			Multivariate		
	β	O.R.	95% C.I.	β	O.R.	95% C.I.
Age (per 10 years)	−0.21**	0.81	0.72, 0.91	−0.32**	0.73	0.61, 0.87
Race/ethnicity (vs. White, non-Hispanic)						
White, Hispanic	−0.04	0.96	0.61, 1.50	0.23	1.26	0.68, 2.33
African-American, non-Hispanic	0.84**	2.32	1.69, 3.17	0.68**	1.97	1.29, 3.03
African-American, Hispanic	0.54	1.71	0.80, 3.64	0.58	1.78	0.73, 4.36
Other	0.59**	1.81	1.26, 2.61	0.66**	1.94	1.17, 3.20
Study Site (vs. Brooklyn)						
Bronx	−1.04**	0.35	0.25, 0.50	−0.79**	0.45	0.29, 0.72
Washington, DC	−0.11	0.90	0.63, 1.29	0.06	1.07	0.67, 1.71
Los Angeles	−0.67**	0.51	0.37, 0.71	−0.50*	0.61	0.38, 0.98
San Francisco	−0.36*	0.70	0.49, 1.00	−0.28	0.76	0.46, 1.24
Chicago	0.05	1.05	0.73, 1.50	−0.04	0.96	0.59, 1.54
Alcohol Consumption (vs. none)						
Light (<3 drinks/wk)	0.41**	1.51	1.30, 1.76	0.41**	1.51	1.20, 1.90
Moderate (3–13 drinks/wk)	0.90**	2.46	1.96, 3.09	0.76**	2.14	1.51, 3.03
Heavier (≥14 drinks/wk)	1.48**	4.37	2.99, 6.40	1.10**	3.00	1.56, 5.77
Drug Use Since Last Visit (vs. none)						
Marijuana only	0.39**	1.47	1.17, 1.85	0.38*	1.46	1.03, 2.07
Use of heroin, cocaine, crack, methadone, or methamphetamine	0.69**	2.00	1.59, 2.52	0.73**	2.08	1.43, 3.02
Ever injected drugs (vs. none)	0.46**	1.58	1.22, 2.05	0.65*	1.92	1.38, 2.69
Self-Perception and Measured Body Fat Changes						
Any Central Fat Gain (vs. no change)	0.15*	1.16	1.02, 1.32	0.41*	1.51	1.15, 1.98
Any Central Fat Loss (vs. no change)	0.25**	1.29	1.10, 1.50	0.31	1.36	0.99, 1.87
Any Peripheral Fat Gain (vs. no change)	0.13	1.14	0.99, 1.31	−0.05	0.95	0.70, 1.30

Variable	Univariate			Multivariate		
	β	O.R.	95% C.I.	β	O.R.	95% C.I.
Any Peripheral Fat Loss (vs. no change)	0.19*	1.21	1.05, 1.39	−0.05	0.96	0.70, 1.30
Change in Weight (per 10 lbs)	0.00	1.00	0.94, 1.06	0.02	1.02	0.89, 1.18
Change in Hip Size (per 5 cm)	−0.03	0.97	0.90, 1.04	−0.08	0.92	0.81, 1.04
Change in Waist Size (per 5 cm)	−0.02	0.98	0.92, 1.04	0.01	1.01	0.91, 1.13
Log10 Viral Load at Previous Visit	0.32**	1.38	1.29, 1.47	0.42**	1.52	1.38, 1.68
Any HAART Switch (vs. none)	−0.17	0.84	0.69, 1.02	−0.63**	0.53	0.39, 0.72

Except for race and study site, all other factors are time-varying.

*P < .05;

**P < .01

Table 3

Adjusted multivariate odds ratios associated with self-reported <95% non-adherence to HAART (n=1,671)

Variable	β	O.R.	95% C.I.
Self-Perception of Any Body Fat Change in Specific Body Sites (vs. no change)			
Central Sites			
Abdomen			
Fat Gain	0.43**	1.53	1.20, 1.95
Fat Loss	0.14	1.15	0.84, 1.58
Neck			
Fat Gain	0.10	1.11	0.81, 1.51
Fat Loss	0.12	1.13	0.79, 1.61
Chest			
Fat Gain	0.16	1.17	0.94, 1.47
Fat Loss	0.29*	1.34	1.04, 1.72
Peripheral Sites			
Face			
Fat Gain	0.15	1.17	0.93, 1.46
Fat Loss	0.17	1.18	0.95, 1.47
Arms			
Fat Gain	0.33*	1.40	1.11, 1.76
Fat Loss	0.25**	1.29	1.03, 1.60
Legs			
Fat Gain	0.25*	1.29	1.02, 1.62
Fat Loss	0.22*	1.24	1.01, 1.52
Buttocks			
Fat Gain	0.27	1.31	0.99, 1.73
Fat Loss	0.15	1.16	0.90, 1.49

Perception for each anatomic site was assessed in a separate model. In general, models adjusted for age (per 10 years), race/ethnicity, study site, alcohol consumption, drug use since last visit, change in weight (per 10 lbs), log10 viral load at previous visit, and any HAART switch. The models for the abdomen and buttocks were also adjusted for change in waist size (per 5 cm) and change in hip size (per 5 cm), respectively. Except for race/ethnicity and study site, all other factors were time-varying.

* $P < .05$;

** $P < .01$