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Association between obesity and combination antiretroviral therapy (cART) adherence among persons with early-stage HIV infection initiating cART

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Abstract

Background—Obesity is common among people living with HIV (PLWH) and early-stage infection, yet associations with combination antiretroviral (cART) adherence are unclear.

Methods—Among PLWH initiating cART in Uganda and South Africa, body mass index (BMI) was assessed at cART initiation, and cART adherence was monitored in real-time over 12 months. The association of obesity (BMI >=30kg/m^2) with adherence was assessed among non-pregnant participants with CD4>350 cells/mm^3 using fractional regression modeling.

Results—Among 322 participants, median age was 32 years, 70% were female, and 54% were from Uganda. Prevalence of obesity was 12% in Uganda and 28% in South Africa. Mean overall cART adherence was 83% in Uganda and 66% in South Africa. Participants with obesity had higher adherence than those without obesity: +3.6% (p=0.44) in Uganda and +11.4% (p=0.02) in South Africa.

Conclusion—Obesity at cART initiation was common and associated with higher adherence, although only significantly in South Africa.

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Introduction

Obesity is increasing globally[1], including in Africa. For example, In 1975, the prevalence of being overweight was 7.3% and 30.0% in Ethiopia and Algeria, respectively, but has since more than doubled to 20.9% in Ethiopia and 62.0% in Algeria in 2016[2].

Obesity is also increasingly a concern among people living with HIV (PLWH)[3], over two-thirds of whom reside in sub-Saharan Africa[4]. In the modern era with early recognition of HIV infection and the high prevalence of obesity characterized by excess adiposity, rather than wasting, is being seen more commonly among PLWH presenting for treatment[5]. For example, 46% of antiretroviral therapy (ART)-naïve patients in one clinic in South Africa had obesity[6].

Weight gain is commonly seen upon ART initiation due to the reversal of the catabolic state associated with uncontrolled viremia and/or direct effects from some forms of ART[7]. However, the impact of obesity at ART initiation on ART adherence is unclear. Adherence may be negatively affected if PLWH, particularly those who have obesity desire to avoid additional gain weight[8]. On the other hand, adherence may improve if any associated weight gain is viewed as a sign of health[9].

In this paper, we explored associations of obesity at combination ART (cART) initiation with 12-month cART adherence among PLWH initiating therapy with early-stage infection in two diverse settings— rural southwestern Uganda and Cape Town, South Africa.

Methods

Participants, study settings, and procedures

The Measuring Early Treatment Adherence (META) study was a prospective cohort study designed to compare adherence between PLWH initiating cART with early versus late-stage HIV infection. Study details have been previously described[10]. Briefly, participants were PLWH enrolled by convenience sampling from routine ART clinics who had early-stage HIV infection (no symptoms, CD4 counts >350 cells/mm^3) or late-stage HIV infection (CD4 counts <200 cells/mm^3). All participants were treated with once daily tenofovir/emtricitabine/efavirenz as a single tablet. Study visits were conducted at baseline, 6 months, and 12 months and involved questionnaire administration and viral load assessment. cART adherence was monitored using a real-time electronic monitor (Wisepill Technologies, South Africa). Every time the monitor was opened, a date and time stamp was recorded and transmitted over the cellular network. Additionally, the monitor sent a daily “heartbeat” to indicate device functionality. Height and weight were measured at baseline; weight was repeated at 12 months.

Statistical analysis

This analysis included non-pregnant participants with early-stage infection. Pregnant women were excluded because of variable metabolic demands related to fetal development. Our primary outcome was 12-month cART adherence and the primary exposure was obesity at cART initiation. Adherence was calculated as the number of electronic monitor openings

divided by the number of expected openings. Adherence was capped at 100% per day and censored at death. Electronic monitor openings by staff and openings during periods of known device malfunction as reflected by absence of a heartbeat or as reported by the study staff was censored. Obesity was defined as a body mass index (BMI) >=30 and viral suppression as <400 HIV RNA copies/mL. Participants were also considered viremic if they died or were lost to follow-up, or if they missed study visits and had <80% adherence in the month before the missed visit. Analysis was stratified by country because of numerous socio-behavioral differences [12] and restricted to participants with available adherence data.

We used Fisher's exact test to compare categorical variables and the Wilcoxon rank sum test to compare adherence by categorical variables. To assess the effect of obesity on adherence independent of potential confounders identified in prior analyses[10], we first ran a univariable fractional regression model including obesity alongside each potential confounder. We then fit a multivariable fractional regression model including obesity at cART initiation and all confounders for which the p-value in the univariable analysis was <0.2. We also ran linear regression models to assess the incremental impact of BMI. To facilitate interpretation, the estimated regression coefficients were converted to average marginal effects. Modeling was conducted using Stata 13 (StataCorp, USA).

Ethics

Ethical review boards at Mbarara University of Science and Technology, Uganda National Council Science and Technology, the University of Cape Town and Partners Healthcare approved the META study. All participants provided written informed consent.

Results

Baseline characteristics (Table 1).

Of the 904 participants enrolled into the META study, 869 had electronic adherence data, of whom 547 (63%) were excluded because of pregnancy or late-stage HIV infection. Of the remaining 322 participants, 175 (54%) were from Uganda and 147 (46%) from South Africa. Median age was 30 years (interquartile range [IQR] 25, 40) and 34 years (IQR 27, 42), and 118 (65%) and 107 (73%) were female, respectively for Uganda and South Africa. Twenty-one (12%) participants in Uganda and 41 (28%) in South Africa had obesity, respectively. Nine participants (3%), 6 from Uganda and 3 from South Africa, were lost to follow-up and 4 (1%), 1 from South Africa and 3 from Uganda, died. Notably, 64 (37%) and 92 (63%) participants reported severe food insecurity in Uganda and South Africa, respectively (p<0.001). We found a trend toward an association between severe food insecurity and lack of obesity in Uganda (p=0.07), but no association in South Africa (p=0.88; Appendix Table 1).

Obesity by gender and over follow-up.

Among females, the prevalence of obesity was 26% at baseline and 27% after 12 months (p=0.80), while that among males was 5% at baseline and 6% at 12 months (p=0.95). No changes in obesity occurred over time (p>0.05).

cART adherence and viral suppression.

Mean 12-month cART adherence was 83% (standard deviation [SD] 19) and 66% (SD 39), while 156 (89%) and 129 (88%) participants had viral suppression at 12 months, respectively for Uganda and South Africa.

Association of obesity and cART adherence.

At month 12, participants with obesity at cART initiation had numerically higher adherence than those without obesity: +3.6 percentage points (95%CI: −5.5, 12.6; p=0.44) in Uganda and +11.4 percentage points (95%CI: 2.0, 21.0; p=0.018) in South Africa (Table 2; see Appendix Tables 2 and 3 for full models by study site). Each 5-point increase in BMI was associated with higher adherence at both sites: +0.3 percentage points (95%CI: −2.4, 3.1; p=0.82) in Uganda and +3.5 (95%CI: 0.1, 7.0; p=0.046) in South Africa, respectively. Associations were statistically significant for South Africa only.

Association of obesity and viral suppression.

Obesity at cART initiation was non-significantly associated with higher odds of 12 month viral suppression at both sites (aOR:1.7 [95%CI 0.3, 11.1]; p=0.58) and (aOR:3.0 [95%CI 0.6, 14.3], p=0.17) for Uganda and South Africa, respectively.

Discussion

In this analysis of PLWH with early-stage HIV disease, we found obesity at cART initiation was common, particularly in South Africa. Obesity was associated with higher average adherence during the first year of treatment, but only significantly in South Africa. This finding is reassuring in that obesity may not negatively impact cART adherence.

In a qualitative analysis conducted at the South Africa site in this study, participants reported a desire to begin ART early, before physical manifestations of AIDS could show; they wanted to avoid stigma and remain “beautiful”[11]. In Uganda, and among black South Africans, obesity has been associated with good health and wealth, while weight loss can be stigmatizing and is often associated with poor health and adversity[12]. Study participants with obesity may have had a perceived state of better health and social standing that they wished to maintain and thus were more motivated than participants without obesity to remain so by adhering to recommended therapy.

While high adherence is desirable for achieving optimal benefits of ART, the rates of obesity in this population raise concern for poor long-term health outcomes. Alternatively, some data suggest that a traditionally defined “healthy” BMI of 18–25 is actually associated with poor health in low and middle-income countries[13], and a recent study found BMI >30 protective against all-cause mortality in South Africa[14]. Further research in this area is needed. The balance of these associations warrants careful consideration given the widespread, ongoing rollout of dolutegravir across sub-Saharan Africa and its potential association with weight gain. Of note, rates of obesity in this cohort were stable over 12 months, which may reflect the use of efavirenz, not dolutegravir.

We also found high rates of severe food insecurity and obesity, particularly in South Africa, although we did not see a significant association between them. Obesity in South African participants was likely related to cheap, refined, high calorie carbohydrate food staples, like mielie-meal, samp and bread, commonly found in the townships[15]. Food security programs in sub-Saharan Africa have traditionally focused on the quantity of food available; however, as incomes rise and access to low-cost, low-quality food increase, attention may also be needed for the quality of food.

One strength of this study is that adherence was objectively monitored and is therefore less likely biased by social desirability and recall compared with subjective adherence monitoring methods (e.g., self-report). Secondly, the two study sites had considerable variation, enhancing generalizability of our findings. Limitations include a relatively small sample size, which may have constrained the ability to detect differences in adherence by BMI category. However, considering that the prevalence in the general population is 4% and 27% for Uganda and South Africa respectively[2], obesity in our sample was relatively similar to that of the general population. Additionally, the study was observational and findings may be susceptible to unmeasured confounding.

In conclusion, obesity at cART initiation may be associated with higher cART adherence among PLWH and early-stage disease in South Africa. This finding may have particular relevance in light of the dolutegravir expansion across sub-Saharan and associated weight gain. However, it also raises concerns for the adverse health effects associated with obesity. Future studies should consider the role of obesity as a risk factor for health outcomes among PLWH in the region.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1:

Enrolment characteristics Values indicate the number (percentage) or median (IQR).

Characteristic	Uganda (n=175)*			South Africa (n=147)*		
	BMI<30 (n=153)	BMI>=30 (n=21)	p-value	BMI<30 (n=103)	BMI>=30 (n=41)	p-value
Age (years)	30 (25, 39)	37 (26, 45)	0.26	34 (25, 42)	38 (31, 43)	0.05
Female	97 (63%)	20 (95%)	0.002	69 (67%)	37 (90%)	0.004
Efavirenz-based cART	153 (100%)	21 (100%)	-	84 (98%)	31 (97%)	0.99
Married	78 (51%)	7 (33%)	0.16	17 (17%)	13 (32%)	0.07
High school education or more	83 (54%)	11 (52%)	0.99	86 (84%)	35 (85%)	0.99
Literacy in local language	133 (87%)	19 (91%)	0.99	90 (89%)	36 (90%)	0.99
1st HIV+ test >30 days before enrolment	99 (65%)	15 (71%)	0.63	62 (68%)	28 (76%)	0.52
Regular income	20 (13%)	4 (19%)	0.5	53 (52%)	23 (56%)	0.71
Exchange sex for money	12 (8%)	4 (19%)	0.11	2 (2%)	0 (0%)	0.99
Severe food insecurity[a]	60 (39%)	4 (19%)	0.09	64 (62%)	26 (63%)	0.99
Probable depression[b]	33 (22%)	2 (10%)	0.26	47 (46%)	27 (66%)	0.041
Heavy alcohol use[c]	14 (9%)	2 (10%)	0.99	32 (31%)	8 (20%)	0.22
Smokes cigarettes	19 (12%)	1 (5%)	0.47	29 (28%)	3 (7%)	0.007
Use of medication besides cART**	135 (88%)	21 (100%)	0.13	17 (17%)	10 (24%)	0.34
Stigma from concerns about disclosure of cART use[d]	4 (1, 6)	3 (0, 5)	0.47	3 (1, 6)	4 (1, 6)	0.3
Stigma from perceived negative attitudes towards HIV[e]	1 (0, 3)	1 (0, 3)	0.47	3 (1, 4)	3 (0, 5)	0.79

[a] Severe food insecurity was defined according to the Household Food Insecurity Access Scale[16].

[b] Scoring an average of ≥1.75 on the Hopkins Depression Symptoms checklist was considered probable depression[17].

[c] An AUDIT score of ≥3 among females and ≥4 among males was considered heavy alcohol use[18].

[d] Stigma from concerns about disclosure of cART use was scored on a scale of 0 to 5 with higher values indicating more stigma[19]

[e] Stigma from perceived negative attitudes towards HIV was scored on a scale of 0 to 7 with higher values indicating more stigma[19]

* Obesity information was missing for 4 participants; Uganda (n=1) and South Africa (n=3)

** (e.g., sulfamethoxazole/ trimethoprim and anti-TB agents)

Table 2:

Unadjusted and adjusted effect of obesity at cART initiation on 12-month adherence stratified by country.

	Univariable		Multivariable	
Country	**Percentage point change (95% CI)**	**p-value**	**Percentage point change (95% CI)**	**p-value**
Uganda[a]	1.8 (−6.7, 10.3)	0.68	3.6 (−5.5, 12.6)	0.44
South Africa[b]	10.1 (0.3, 19.9)	0.04	11.4 (2.0, 21.0)	0.02

[a]Controlling for age at enrollment, gender, whether first positive HIV test was greater than 30 days prior to enrolment, heavy alcohol use, cigarette use, exchange of sex for money, use of medication other than cART (e.g., sulfamethoxazole/trimethoprim and anti-TB agents), and stigma from concerns about disclosure of ART status.

[b]Controlling for structural barriers to health care access, stigma from concerns about disclosure of ART status and stigma from perceived negative attitudes towards HIV.