Caffeine Intake and Its Association with Body Composition Measures and Macronutrient Intakes in People Living with HIV in the Miami Adult Studies on HIV Cohort

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Background: Caffeine acts as an anorexic agent, increases energy expenditures, and decreases total body fat mass, and could be detrimental to people living with HIV (PLWH). The objective of this study was to explore the relationship between caffeine consumption, body composition measures (fat mass, body mass index [BMI], and lean body mass [LBM]), nutrient intakes, CD4 counts, and HIV viral load in PLWH.

Methods: A convenience sample of 130 PLWH was recruited and followed for 3 months. Caffeine intake, body composition measures, and nutrient intakes were collected using Modified Caffeine Consumption Questionnaire, bioimpedance analyses, and 24-hour dietary recalls. Linear regressions were used to analyze the baseline data for relationships between these variables. Linear mixed models (LMMs) were used to determine the overtime changes.

Results: In baseline, linear regression analysis, higher caffeine consumption was associated with lower fat mass ($\beta = -0.994$, $p = 0.042$). However, BMI and LBM did not show any significant association with caffeine intake. LMM analysis showed that the association between caffeine intake and fat mass strengthened overtime ($\beta = -1.987$, $p = 0.035$). Baseline linear regression analysis showed that higher caffeine intake was significantly associated with lower caloric intakes from fat ($\beta = -1.902$, $p = 0.044$) and lower total caloric intake ($\beta = -1.643$, $p = 0.042$). However, LMM analysis showed that these associations diminished and lost significance overtime. There were no associations between body composition measures, nutrient intakes, CD4 counts, and HIV viral load.

Conclusions: Caffeine intake adversely affected dietary intakes of macronutrients and total fat mass. Therefore, caffeine, a known anorectic, should be regulated in PLWH.

Keywords: caffeine, body composition, macronutrient, people living with HIV

Introduction

SIGNIFICANT IMPROVEMENTS in availability and accessibility of combination antiretroviral therapy (ART) medications and lack of an effective vaccine¹ have made AIDS a chronic disease with increasing life expectancy.²

According to the Centers for Disease Control and Prevention and Florida Department of Health estimates in 2014, there were about 1.1 million people living with HIV (PLWH) in the United States, and 26,760 of them were living in Miami-Dade, currently the county with the highest incidence in the United States.^{3,4} Most of the PLWH in

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Miami live in marginalized neighborhoods with limited resources.⁵ Many socioeconomic factors, such as homelessness, illegal commercial sex, drug abuse, alcohol addiction, tobacco use, and criminalization, act as barriers toward access to nutritious foods and supplements.^{6–11} Although the majority of the Miami Adult Studies of HIV (MASH) cohort,^{12,13} from which our participants were recruited, received social security benefits and some forms of food assistance, many experienced food insecurity.⁹ Food insecurity and decreased food intake are associated with uncontrolled HIV viral load and increased mortality, even among participants receiving combination ART.^{14,15} Similarly, weight loss and lower body mass index (BMI) are associated with faster disease progression in terms of lower CD4 cell counts and uncontrolled HIV viral load even among those receiving ART.^{16–18}

Caffeine consumption is associated with anorexic, lipolytic, and thermogenic effects due to its inhibitory action on the cyclic adenosine monophosphate (cAMP) degradation pathway, as well as increased cAMP generation by stimulation of beta-adrenergic receptors.¹⁹ In a double-blind, placebo-controlled study on healthy volunteers, caffeine intake produced a positive and dose-dependent increase in resting energy expenditures (REEs) after controlling for plasma lactate levels and plasma triglyceride levels.²⁰ In another double-blind, placebo-controlled study, caffeine increased REE indicated by increased levels of serum norepinephrine, glycerol, free fatty acids (FFA), and basal metabolic rate.²¹ Similar effects were reported in another study where caffeine produced an increased REE by increasing the resting oxygen uptake.²² Caffeine also produced a twofold increase in lipid turnover, increased thermic effect, and increased oxidative FFA disposal compared to placebo by 2.3 times, indicating an increased REE and lipid breakdown.²²

Studies show that caffeine acts as an anorexic agent, increases energy expenditures by unknown mechanisms, and decreases total body fat mass by activating hormone-sensitive lipase, which increases lipolysis and fat mobilization from the adipose tissue. Such effects could be detrimental to PLWH, because many of them already experience food scarcity and insecurity.⁹ Despite these effects, studies relating caffeine and its nutritional effects in PLWH are scarce. Therefore, this study explored the effects of caffeine consumption on body composition measures and macronutrient intakes in a group of PLWH recruited from the MASH cohort. In addition, this study also evaluated the net effects of body composition measures and macronutrient intakes on markers of HIV disease progression (CD4 counts and HIV viral load).

Materials and Methods

Study design and setting

A convenience sample of 130 participants was recruited from the MASH cohort, which consisted of 803 HIV-

positive participants, followed for more than 10 years at the Florida International University (FIU) Research Clinic in the Borinquen Health Care Center (BHCC). The BHCC provides a comprehensive range of health and social services to a culturally diverse low-income community. The recruitment for this study took place from February to July 2014 and included a baseline and 3-month follow-up visits. The participants received \$5 as partial reimbursement for their time and effort, for each of the two visits. To obtain a study sample of 128 participants, as estimated in our sample size calculations, we recruited and enrolled 130 participants. Data collected during the baseline and 3-month visits were used for analyses of descriptive and inferential statistics. The inclusion criteria for this study were as follows: (1) enrollment in the MASH cohort; (2) currently on ART; and (3) willingness to participate in this study consisting of two visits. The exclusion criteria were as follows: (1) cardiovascular abnormalities and (2) morbid medical conditions such as uncontrolled hypertension, anemia, chronic inflammatory diseases, or malabsorption syndromes. The FIU Institutional Review Board approved the study protocol and research procedures. Each participant provided written informed consent to participate in this study.

Measures

Demographics and substance use. Demographic and substance use characteristics were collected by the MASH cohort studies and included age, gender, ethnicity, education, income, and substance use such as tobacco use, alcohol consumption, and recreational drug use.

Caffeine Consumption Questionnaire. The Modified Caffeine Consumption Questionnaire (MCCQ) developed by Preston *et al.* was used.¹⁹ This questionnaire is easy to understand, compact, organized, and reported adequate compliance, validity, and reliability.¹⁹ It includes a total of 21 sources of caffeine classified into three groups: beverages, over-the-counter medications, and prescription medications. Total caffeine consumption per day was derived by adding all the individual sources. For both naturally occurring and artificially added caffeine sources, The International Classification of Diseases (ICD) manual considers caffeine consumption above 250 mg/day to be associated with many psychological and behavioral side effects, although it is inconclusive whether such effects would be uniformly applicable to the general population.^{23,24} The Diagnostic and Statistical Manual of Mental Disorders (DSM-5) considers consumption below 250 mg/day to be generally safe, but above this level, consumption has been associated with many adverse effects such as withdrawal, addiction, irritability, and craving.²⁵ In this study, caffeine consumption was categorized as safe and low (≤ 250 mg/day) and high (> 250 mg/day) based on these recommendations.

Nutritional status assessment

Macronutrient intakes. Twenty-four-hour dietary recalls were used to estimate daily dietary and macronutrient consumption by the participants. During both the study visits, participants were queried about foods and beverages consumed on the day before the visit. In addition, details on cooking methods, amount consumed, additional ingredients, and seasonings were also recorded. Food brands were also recorded to confirm the validity of the information obtained. Food models and measuring cups were used to ensure accuracy of the amounts and volumes consumed, and to provide cues for better recall of consumed foods. Nutribase Professional Software version 9 (Cybersoft, Inc., 2011) was used to analyze the 24-hour intakes, to obtain an estimation of the kilocalories consumed through the macronutrients.

Body composition measures. Height was recorded to the nearest 0.5 inch after removing shoes and socks. Weight was measured to the nearest 0.1 lbs. using a standard weighing machine. Participants were requested to remove their watches, shoes, mobile phones, or other heavy items before being weighed. The weight and height, along with age, were entered into the bioimpedance instrument (Biodynamics-450) to obtain several body composition measures, including extracellular mass, lean body mass (LBM), fat mass, BMI, and intracellular and extracellular fluid levels.²⁶

CD4 count and HIV viral load. CD4 cell count and HIV viral load were used as parameters of HIV disease progression. The MASH cohort studies collected and recorded the laboratory reports for CD4 counts (FACS-Canto II Flow Cytometer; BD Biosciences, San Jose, CA) and HIV viral load (RealTime HIV-1 PCR; Abbott Molecular, Des Plaines, IL), after appropriate medical release forms were signed by the participants. In the analyses, CD4 count and HIV viral load were considered continuous variables and were transformed into the CD4 square root and $\log_{10}$ HIV viral load to ensure better model fit criteria.

Statistical analyses

SPSS version 23 for Windows (IBM Corp, Armonk, NY) was used for data analyses. Descriptive statistics and frequencies were used to describe the demographic characteristics and substance use, and were expressed in terms of means, standard deviations, and percentages. The demographics and substance use variables were separated based on low and high intakes of caffeine. T-tests and chi-square tests were used to compare the differences in demographics and substance use characteristics, macronutrient intakes, and body composition measures. Paired sample *t*-tests were used to understand the changes in caffeine, macronutrient intakes, and body composition measures between the baseline

and 3-month visits. Baseline linear regression analyses were used to estimate the strength of the association between caffeine intake and body composition measures, and macronutrient intake. Baseline linear regression was also used to estimate the strength of the association between body composition measures and macronutrient intake, and markers of HIV disease progression (CD4 counts and HIV viral load). Linear mixed models (LMMs) were used to determine the changes in these associations over time. For parameter estimation in LMMs, Restricted Maximum Likelihood was used. For both linear regressions and LMM analyses, we initially used crude models and subsequently adjusted for covariates such as age, gender, race/ethnicity, grades of schooling, income, drug use, alcohol use, and smoking. These covariates were also tested for significant associations with the outcome variables using bivariate analysis before being incorporated into the models. Adjusted models included nonmissing values for all independent variables included in the models. Statistical significance was set at $p < 0.05$ for all the analyses.

Results

Demographic and substance use characteristics

A total of 130 participants were included in the study and 79 (60.8%) were men. The mean age of the sample was 47.8 ± 6.3 years. Most of the participants were African Americans (75.4%), Hispanics constituted 16.9%, whites constituted 5.4%, and other races were 2.3%. Less than one fourth (23.8%) of the participants had college education, while 45.4% were high school graduates, and 30.8% has some form of primary education. The mean income of the sample was $\$495.9 \pm 465.8$ per month. There were no significant differences in any demographic and substance use variable between low and high levels of caffeine consumption in both the baseline and follow-up visits (Table 1). Sixty-four percent of the participants reported smoking cigarettes within the past 6 weeks of their scheduled baseline visits, 57.9% reported alcohol use, and 48.2% tested positive for recreational drug use. All participants were on ART during the entire duration of the study.

Caffeine consumption from different sources

The mean total caffeine consumption from all sources was 337.6 ± 304.9 mg/day at baseline visit and 281.0 ± 260.8 mg/day at follow-up visit. Coffee constituted the largest source of caffeine, and mean consumption levels were 161.2 ± 194.9 mg/day at baseline and 190.4 ± 205.0 mg/day at follow-up visit. Caffeinated soft drinks constituted the second largest source of caffeine and mean consumption levels were 63.2 ± 92.9 mg/day at baseline and 29.6 ± 83.7 mg/day at follow-up visit. There were no significant differences between baseline and follow-up visits with respect to total caffeine consumption or caffeine from most of the sources.

TABLE 1. DEMOGRAPHIC CHARACTERISTICS OF THE PARTICIPANTS BY CAFFEINE CONSUMPTION LEVELS (N=130)

Characteristics	Low caffeine intake (≤ 250 mg/day)	High caffeine intake (>250 mg/day)	Total	p
Age, years (mean $\pm$ SD)	47.5 $\pm$ 6.8	48.0 $\pm$ 6.1	47.8 $\pm$ 6.3	0.706
Gender, n (%)				0.857
Male	40 (61.5)	39 (60.0)	79 (60.8)	
Female	25 (38.5)	26 (40.0)	51 (39.2)	
Ethnicity, n (%)				0.057
White	3 (4.6)	4 (6.2)	7 (5.4)	
Hispanic	7 (10.8)	15 (23.1)	22 (16.9)	
Black	55 (84.6)	43 (66.2)	98 (75.4)	
Other	0 (0.0)	3 (4.6)	3 (2.3)	
Education, years, n (%)				0.202
<12	24 (36.9)	16 (24.6)	40 (30.8)	
12	29 (44.6)	30 (46.2)	59 (45.4)	
>12	12 (18.5)	19 (29.2)	31 (23.8)	
Income in dollars per month (mean $\pm$ SD)	464.0 $\pm$ 419.6	527.3 $\pm$ 508.6	495.9 $\pm$ 465.8	0.442
Smoking cigarettes, n (%)	39 (60.9)	41 (66.1)	80 (63.5)	0.582
Alcohol use, n (%)	36 (56.3)	37 (59.7)	73 (57.9)	0.721
Drug use, n (%)	25 (43.9)	28 (52.8)	53 (48.2)	0.445
Marijuana, n (%)	21 (32.3)	23 (35.4)	44 (33.8)	0.853
Cocaine, n (%)	19 (29.2)	22 (33.8)	41 (31.5)	0.706
Other drugs, n (%)	6 (10.5)	4 (7.5)	10 (9.1)	0.744

p-Values correspond to χ^2 tests for categorical variables and *t*-test for continuous variables.

However, there was significant decrease in consumption of caffeinated soft drinks ($p < 0.001$), energy drinks ($p = 0.005$), and hot cocoa ($p = 0.020$) from baseline to the follow-up visits (Table 2).

Dietary intakes by caffeine consumption status

During the baseline visit, carbohydrate ($p = 0.048$), protein ($p = 0.046$), and fat ($p = 0.048$) intakes were significantly lower in participants consuming high levels when compared to low levels of caffeine per day (Table 3). Similarly, during the follow-up visit, carbohydrate ($p = 0.042$), protein ($p = 0.017$), fat ($p = 0.026$), and total caloric ($p = 0.017$) intakes were significantly lower in high caffeine consumers compared to low caffeine consumers. There were no significant differences in any macronutrient intakes between the baseline and follow-up visit (Table 3).

Relationship between caffeine consumption and body composition measures

Baseline linear regression analysis showed that higher caffeine consumption was associated with lower fat mass ($\beta = -0.994$, $p = 0.042$) after adjusting for covariates. However, BMI and LBM did not show significant associations with caffeine intake. LMM analysis showed that the association between caffeine intake and fat mass strengthened overtime ($\beta = -1.987$, $p = 0.035$), after adjusting for the same covariates (Table 4).

Relationship between caffeine consumption and dietary intakes

Baseline linear regression analysis showed that higher caffeine intake was significantly associated with lower calories from fat ($\beta = -1.902$, $p = 0.044$) and lower total caloric intake ($\beta = -1.643$, $p = 0.042$), after adjusting for

TABLE 2. MEAN CAFFEINE INTAKE FROM DIFFERENT SOURCES (N=130)

Food source	Baseline	Follow-up	p
Coffee (mean $\pm$ SD)	161.2 $\pm$ 194.9	190.4 $\pm$ 205.0	0.206
Decaffeinated coffee (mean $\pm$ SD)	0.83 $\pm$ 9.2	0.0 $\pm$ 0.4	0.329
Espresso (mean $\pm$ SD)	14.4 $\pm$ 64.3	13.9 $\pm$ 57.8	0.942
Tea (mean $\pm$ SD)	34.7 $\pm$ 64.3	31.5 $\pm$ 59.3	0.640
Green tea (mean $\pm$ SD)	7.3 $\pm$ 62.9	4.2 $\pm$ 21.6	0.594
Energy drinks (mean $\pm$ SD)	46.3 $\pm$ 134.4	9.6 $\pm$ 65.3	0.005
Hot cocoa (mean $\pm$ SD)	1.0 $\pm$ 5.0	0.0 $\pm$ 0.0	0.020
Caffeinated soft drinks (mean $\pm$ SD)	63.2 $\pm$ 92.9	29.6 $\pm$ 83.7	<0.001
Chocolate candy bars (mean $\pm$ SD)	3.6 $\pm$ 13.8	2.0 $\pm$ 17.9	0.402
Anacin (mean $\pm$ SD)	0.2 $\pm$ 2.8	0.0 $\pm$ 0.0	0.319
Appetite control pills (mean $\pm$ SD)	4.6 $\pm$ 39.1	0.0 $\pm$ 0.0	0.181
Total (mean $\pm$ SD)	337.6 $\pm$ 304.9	281.0 $\pm$ 260.8	0.890

TABLE 3. MEAN NUTRIENT INTAKE AND BODY COMPOSITION MEASURE BY LEVELS OF CAFFEINE CONSUMPTION (N=130)

Variables	Baseline			Follow-up		
	Low caffeine intake	High caffeine intake	p	Low caffeine intake	High caffeine intake	p
BMI (kg/m ²)	27.2 ± 5.0	27.3 ± 6.2	0.919	26.1 ± 7.0	27.5 ± 6.7	0.280
LBM (lb)	129.8 ± 27.2	127.0 ± 24.0	0.535	121.1 ± 23.1	119.0 ± 24.9	0.634
Fat mass (lb)	49.3 ± 26.3	48.0 ± 27.1	0.789	53.9 ± 26.2	59.5 ± 25.6	0.219
Total carbohydrate (g)	341.8 ± 133.4	259.1 ± 132.2	0.048	2100.5 ± 1127.8	1858.2 ± 932.0	0.042
Total protein (g)	94.8 ± 54.5	85.2 ± 40.8	0.04	255.2 ± 152.9	151.3 ± 116.7	0.017
Total fat (g)	170.9 ± 44.5	93.4 ± 48.4	0.048	86.4 ± 42.1	43.4 ± 37.8	0.026
Total calorie (kcal)	1911.8 ± 1045.6	2038.3 ± 945.8	0.791	183.7 ± 68.7	77.5 ± 56.4	0.017

BMI, body mass index; LBM, lean body mass.

covariates. However, calorie from protein and carbohydrates did not show significant associations with caffeine intake. LMM showed that these associations diminished and became nonsignificant over time (Table 4).

Relationship between body composition and macronutrient intake and CD4 count and HIV viral load

Baseline linear regression showed that body composition measures were not associated with calorie consumption, CD4 cell count, and HIV viral load. LMM showed that there were no associations between these variables over time (Table 5).

Discussion

In our study, we found that caffeine intake adversely affected macronutrient intake and body fat mass. All participants had incomes below the poverty level and more than half of them were consuming alcohol and smoking cigarettes, and had positive urine toxicology result for recreational drugs. Poverty, substance abuse, and dependence could have adversely influenced their dietary in-

take and food purchasing potential, and caffeine could have additionally worsened these characteristics.

A study done among 459 male and 212 female PLWH found that food insecurity was associated with poverty and substance use.²⁷ One in four participants in this study reported alcohol and tobacco purchase with resources allocated for food.²⁷ In our study, caffeine consumption was associated with decreased dietary intakes of macronutrients and decreased fat mass. Caffeine also contributed to the weight loss effects of other powerful anorectic agents such as cocaine. These adverse associations of caffeine were superimposed on the already inadequate diet recorded for most participants due to substance use and socioeconomic factors. Adverse effects of caffeine on energy deficits and weight loss were observed in many non-HIV-infected populations.^{28–31} In a long-term follow-up study of 18 years, conducted in 1333 males and 4085 females with type-2 diabetes, there was a strong association between caffeine consumption (>4 cups/day, which is approximately >240 mg caffeine/day) and weight loss after controlling for age, body weight, insulin and anti-diabetic drugs, physical activity, and lifestyle factors.³¹ Further analysis of the

TABLE 4. LINEAR MIXED-MODEL ANALYSIS OF OVERTIME CHANGES IN BODY COMPOSITION MEASURES AND NUTRITIONAL INDICATORS DUE TO CAFFEINE CONSUMPTION (N=130)

Variables	Unadjusted ^a			Adjusted ^{b,c}		
	β	SE	p	β	SE	p
Body composition measures						
BMI (kg/m ²)	-1.310	0.870	0.647	0.987	0.910	0.532
LBM (lb)	-0.477	0.332	0.815	-0.363	0.377	0.338
Fat mass (lb)	-0.001	0.003	0.958	-1.987	0.910	0.035
Calorie consumption						
Calorie from protein (kcal)	0.013	0.049	0.784	0.039	0.058	0.506
Calorie from carbohydrates (kcal)	-0.099	0.108	0.361	-0.079	0.116	0.497
Calorie from fats (kcal)	-0.895	0.991	0.367	-0.317	0.118	0.789
Total energy (kcal)	-0.933	0.821	0.257	-0.402	0.942	0.670

^aModel: -2 Restricted Log Likelihood = 1832.170; AIC = 1836.170; Schwarz's Bayesian Information Criteria (SBIC) = 1842.716.

^bModel: -2 Restricted Log Likelihood = 1252.041; AIC = 1256.014; Schwarz's Bayesian Information Criteria (SBIC) = 1262.539.

^cModel controlled for age, gender, cigarette smoking, alcohol use, and drug use.

AIC, Akaike's information criteria.

TABLE 5. LINEAR MIXED-MODEL ANALYSIS OF OVERTIME CHANGES IN CD4 CELL COUNT AND HIV VIRAL LOAD DUE TO CHANGES IN BODY COMPOSITION MEASURES AND MACRONUTRIENT CONSUMPTION ($N=130$)

Variables	Unadjusted ^a			Adjusted ^{b,c}		
	β	SE	p	β	SE	p
CD4 cell count						
BMI (kg/m ²)	0.151	0.076	0.068	0.972	0.486	0.567
LBM (lb)	0.216	0.189	0.255	0.266	0.225	0.106
Fat mass (lb)	0.592	0.176	0.052	0.936	0.223	0.056
Calorie from protein (kcal)	-0.786	0.153	0.609	-0.987	0.155	0.994
Calorie from carbohydrates (kcal)	-0.915	0.757	0.347	-0.934	0.857	0.517
Calorie from fats (kcal)	0.930	0.765	0.226	0.965	0.794	0.827
Total energy (kcal)	0.219	0.097	0.625	0.901	0.710	0.624
HIV viral load						
BMI (kg/m ²)	-0.463	0.026	0.324	-0.013	0.018	0.322
LBM (lb)	-0.304	0.380	0.793	-0.532	0.483	0.261
Fat mass (lb)	-0.810	0.472	0.456	-0.724	0.485	0.314
Calorie from protein (kcal)	-0.214	0.134	0.740	-0.189	0.035	0.922
Calorie from carbohydrates (kcal)	0.218	0.137	0.155	0.515	0.192	0.421
Calorie from fats (kcal)	0.974	0.547	0.622	-0.834	0.851	0.851
Total energy (kcal)	-0.158	0.121	0.253	-0.586	0.123	0.845

^aModel: -2 Restricted Log Likelihood=1129.609; AIC=1133.609; Schwarz's Bayesian Criteria (BIC)=1139.868.

^bModel: -2 Restricted Log Likelihood=1136.666; AIC=1140.666; Schwarz's Bayesian Criteria (BIC)=1146.937.

^cModel controlled for age, gender, cigarette smoking, alcohol use, and drug use.

same study found a dose-response relationship between caffeine intake and weight loss.³¹ In a systematic review of 20 studies on the protective effects of caffeine in diabetes, 12 studies reported weight loss due to caffeine consumption.²⁸ This review also reported an estimated 100 kcal/day increased energy deficits due to habitual consumption of 7 cups of coffee (~400 mg caffeine/day).²⁸ Eight of these 20 studies also reported a dose-response relationship between caffeine intake and weight loss.²⁸

Our study also found that total fat mass was adversely affected by caffeine consumption. Probable mechanisms include increased basal energy expenditures (BEE) and the thermogenic effects of caffeine.³² Similar mechanisms were reported in a study done in young healthy women, where caffeine increased BEE, even in the presence of genetic abnormalities predisposing to decreased BEE.³² The Arg allele in the beta-3 adrenergic receptor gene (beta-3-AR) is a marker for obesity-related traits, and mutations in this gene leads to decreased BEE.^{29,32} In a group of women showing beta-3-AR Trp64Arg abnormalities and consequently decreased BEE, 250 mg/day of caffeine produced a significant increase in BEE measured by indirect open-circuit calorimeter at four intervals during the day.³² This study showed that caffeine, independent of genetic predispositions to gain weight, increased REE leading to significant weight loss.³²

Our study did not find any association between body composition measures and CD4 cell count and HIV viral load. However, higher total fat mass and higher BMI have been associated with better immunological and virological profiles. Such beneficial effects were reported by Jones *et al.*,¹⁷ in a study among 871 female

PLWH followed for 3 years. Cross-sectional analysis, survival analysis, and longitudinal analysis revealed that, all five HIV disease severity outcomes such as CD4 cell count and viral load, time to first occurrence of CD4 cell count ≤ 200 cells/mm³, first occurrence of CD4 cell count ≤ 100 cells/mm³, first occurrence of other infection/malignancy, and HIV-related deaths were significantly delayed in women in the obese group (BMI ≥ 35 kg/m²).¹⁷ A longitudinal study conducted among 125 HIV-1-seropositive drug users on ART showed that nonobese individuals reported a 25% decline in CD4 cell counts, compared to 18% decline in obese patients ($p < 0.004$), over a period of 18 months.³³ This study also showed that BMI was inversely associated with time toward progression to AIDS and death, after controlling for covariates such as ART and drug use.³³ This study states that HIV infection constitutes a chronic hypermetabolic state with increased demands on existing fat reserves, which if not replenished, would aggravate the process of wasting.³³ Many other studies have also reported that resting metabolic rate was significantly higher in HIV-positive patients compared to healthy controls, leading to energy deficits and wasting.³⁴⁻³⁶ The importance of preserving healthy BMI in PLWH is adequately emphasized in a review by Langford *et al.*,³⁷ which summarized that BMI < 20.3 kg/m² in men and < 18.5 kg/m² in women were strong indicators of mortality due to HIV in many racially diverse populations. This review also stated that BMI values 17-18 and < 16 kg/m² increased the risk for progression to AIDS by twice and five times, respectively, and that BMI < 18.5 kg/m² was as useful

as clinical staging and serological and immunological markers for decisions about ART initiations.³⁷ All these studies justify the need to prevent weight loss, especially loss of fat mass in HIV-positive patients. Therefore, caffeine, a known anorectic agent, should be regulated in PLWH reporting decreased BMI, fat mass, and signs of wasting.

This study has some limitations. This study enrolled a consecutive convenient sample of 130 HIV-positive participants and the generalizability is weak. Participating in the baseline could also have influenced the outcomes in the follow-up visit, as the participants could have been affected by interpersonal expectancy bias. The 24-hour dietary recall used for assessing nutrient consumption is a self-reported measure and subject to memory and recall biases. Although all participants were recommended multivitamin supplements during their regular follow-ups with their physicians, we could not specifically obtain data about compliance with multivitamin supplements. In addition, the effect of caffeine is influenced by genotypic variations in metabolizing enzymes, resulting in individual differences for same levels of consumption. However, we did not do genotyping studies to understand these differences, thus limiting our validity.

Conclusions

Large-scale studies should be conducted with controlled dietary and lifestyle factors, as well as standardized study settings to overcome the limitations of our study. Although our findings showed that caffeine intake adversely affected dietary intakes of macronutrients and total body fat mass, these findings should be confirmed by large-scale studies.

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Author Disclosure Statement

No competing financial interests exist

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