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Association of Physical Activity with Lipodystrophy Syndrome in HIV-Infected Patients

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Abstract

Highly Active Antiretroviral Therapy (HAART) has increased life expectancy of HIV-infected patients, but may also increase triglyceride and cholesterol levels, triggering lipodystrophy syndrome. Physical activity may prevent or attenuate such adverse effects, but it has not been fully evaluated in HIV-infected patients. This cross-sectional study aimed to investigate the association between physical activity and lipodystrophy syndrome in HIV-infected individuals, 18 years or older. Physical activity was evaluated by the short version of the International Physical Activity Questionnaire. Lipodystrophy was verified by at least two reporting of changes in different parts of the body, or directly assessed, categorized as lipoatrophy or lipohypertrophy. Among 1,240 participants, 46% had lipohypertrophy, which was independently associated with insufficient physical activity in men, but not in women. The prevalence of lipoatrophy was 53.2%. Metabolic parameters were higher among individuals on HAART, in comparison to HAART-naive patients. In conclusion, HAART-naive physically active individuals had lower metabolic profile than among insufficiently active.

Keywords: HIV/AIDS; Lipodystrophy; Physical activity; Exercise; Lifestyle

Introduction

Highly Active Antiretroviral Therapy (HAART) has significantly changed the morbidity and quality of life among HIV-infected patients [1]. However, HIV-associated lipodystrophy syndrome is among the adverse effects of HAART, characterized by atrophy in the peripheral regions (fat reduction in the face, arms and legs) and lipohypertrophy in the central region (fat accumulation in the chest, abdomen, neck and dorsocervical region) [2-4], which can be presented alone or combined (mixed lipodystrophy) [2,3]. The syndrome may also increase the levels of triglycerides, total cholesterol, Low-Density Lipoprotein fraction (LDL) and glucose, and reduce the levels of High-Density Lipoprotein (HDL) [4,5].

Although HIV-associated lipodystrophy syndrome is clearly influenced by the use of HAART, reverse transcriptase inhibitors are strongly associated with lipoatrophy and protease inhibitors to lipohypertrophy and lipid disorders. The pathophysiology of HIV-associated lipodystrophy syndrome is not yet fully elucidated though. Factors associated with lipodystrophy include gender, age, class of antiretroviral and duration of HAART use [6]. There are reports of these changes among HIV-individuals that are not under antiretroviral treatment [4]. Thus, AIDS is now classified as a chronic disease, resulting in increased cardiovascular risk [7].

Behavioral changes and lifestyle, such as diet and physical activity (and/or exercise), smoking cessation and reduction of alcohol consumption could be non-pharmacological strategies for the prevention or treatment of HIV lipodystrophy syndrome. The prevalence of smoking is high among HIV-infected persons [8], and this habit causes serious health problems, such as cardiorespiratory disorders that can accelerate the progression to AIDS, i.e., the installation of opportunistic diseases [9], reducing levels of CD4 count and viral load increase [10,11]. Healthy lifestyle habits are important for the general population and are also relevant for HIV-infected individuals [8]. However, exercise can worsen lipoatrophy [2,6], even though it has beneficial effects on lipohypertrophy and lipid levels [9-12]. Generally, among people infected with HIV or not, there are reports on the fact that women have a higher accumulation of abdominal fat, and men are more physically active, which is why the data should be analyzed by gender [13,14].

This study aimed to investigate the association between physical activity and HIV-associated lipodystrophy syndrome and metabolic profile.

Methods

A cross-sectional study enrolled HIV-infected male and female patients, aged 18 years or older, between 2006 and 2008, attending a secondary hospital, which is a reference center for HIV-testing and outpatient treatment for HIV, in Porto Alegre, southern Brazil. Patients under the influence of illicit drugs or alcohol at the time of the interview were excluded, as well as pregnant women and subjects with participation restrictions due to mental disabilities or restraints

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of freedom. The Institution Review Board approved the protocol and patients signed an informed consent to participate.

Study enrollment and definitions

Patients were interviewed using a standardized questionnaire during the routine visit for HIV treatment, including questions pertaining to demographic (age, gender, race), socioeconomic (education) and lifestyle (physical activity, smoking and alcohol consumption) characteristics by certified interviewers. Clinical data (use of highly active antiretroviral therapy and duration of HIV-infection) and laboratory information (CD4 count and HIV viral load) were obtained from medical records, for the three months prior to the interview. Patients were considered on highly active antiretroviral therapy (HAART) use, if they were taking three antiretroviral drugs; naïve-treatment patients were those who had never used any antiretroviral drug. Viral load below 50 copies/mL HIV RNA was considered undetectable. Race was self-reported and participants were categorized as Whites or non-Whites. Education was measured by years of schooling, categorized as high school education (yes or no). Smokers were characterized by lifetime consumption of at least 100 cigarettes, and pack-year of smoking was calculated by multiplying the number of packs smoked per day by the number of years smoked [15].

Weight, height, waist circumference, hip, arm and neck, and three facial skinfolds-infraorbital, submandibular and buccal-measurements were performed in duplicate and the average was used for analysis. Body circumference measurements were performed using inelastic anthropometric tape. The midpoint between the anterior superior iliac spine and iliac crest and the inferior costal rib was used for waist circumference. Hip circumference was measured at its largest area. Neck circumference was performed with the patient sitting, with the area uncovered, positioning the tape over the Adam's apple. Circumference of the arm was measured at the midpoint between the acromion and olecranon, with the limb positioned at 90 degrees. Facial skinfolds (infraorbital, buccal and submandibular) were measured using a Cescorf brand adipometer.

To identify alcohol consumption abuse, even occasional, binge drinking category was created for individuals with intake of at least five drinks of any alcoholic beverage on a single occasion.

Inquiries on self-awareness of body changes after HIV infection diagnosis were made. The questions were asked to determine whether the patients had noticed changes in body fat distribution, increase or decrease in general and in specific parts of the body.

Lipodystrophy was determined by the presence of at least two changes in different parts of body, using self-perception and objective measurements. Self-perception of body changes was based on increase or decrease of body fat, or on body parts, including face, dorsocervical fat pads, stomach, chest or breasts; or on the reduction of arms, legs, waist, buttocks, and sunken cheeks in the face. Objective measurements included neck, waist, and hip circumferences, and skin-fold thicknesses on the face. Lipohypertrophy and lipoatrophy were determined by a combination of at least two measurements at 90th and 10th percentiles, respectively, and/or positive signs based on patient's self-perception.

Patients for whom information lipid profile-total cholesterol, High Density Lipoprotein (HDL) fraction and Low Density Lipoprotein (LDL), triglycerides and fasting glucose–could not be obtain from medical records of the examinations performed over the last two months, were given request for laboratory examinations. Blood sample was collected after a 12-hour fasting period, and all examinations were performed at the same clinical laboratory.

Physical activity

Physical activity was evaluated by the short version of the International Physical Activity Questionnaire (IPAQ), and participants were categorized as active if they had performed ≥150 minutes of moderate to vigorous intensity physical activity along five days in the previous week or as insufficiently active otherwise.

Statistics

Epi Info version 3.5.1 (Centers for Disease Control) was used for double data entry. Statistical analysis was performed using the Statistical Package for Social Sciences (SPSS for Windows v 16; Chicago, IL, USA). Prevalence ratio (95%CI) was calculated for characteristics associated with physical activity, crude and subsequently adjusted for potential confounding variables, using modified Poisson regression models. Confounding factors were selected among variables associated with physical activity, in the bivariate analysis (P value <0.10), or those described as such in the literature (Age, education and alcohol consumption abuse).

Results

A total of 1,240 HIV-infected patients were enrolled; mean age was 39.1 ± 10.1 years; 50.6% were men, aged 40 ± 9.6 years, 49.4% women, whose average age was 38.2 ± 10.4 years.

The prevalence of lipoatrophy was 53.2% and lipohypertrophy was 46% among HIV-infected individuals.

The characteristics of the participants, classified according to the presence or absence of lipohypertrophy, are shown in table 1.

Of the total study participants, females, non-Whites, non-smokers,

	Total (n=1,240)	Prevalence of Lipohypertrophy		
		Overall (n=1240)	Men (n=628)	Women (n=612)
Gender				
Men	628 (50.6)	242 (38.5)	-	-
Women	612 (49.4)	328 (53.6)	-	-
P value		<0.001		
Age (years)				
18-34	471 (38.0)	211 (44.8)	69 (32.7)	142 (67.3)
35-49	591 (47.7)	266 (45.0)	135 (50.8)	131 (49.2)
50-78	178 (14.3)	93 (52.2)	38 (40.9)	55 (59.1)
P value		0.2	0.3	0.3
Skin color				
White	692 (55.8)	298 (43.1)	148 (49.7)	150 (50.3)
Non-white	548 (44.2)	272 (49.6)	94 (34.6)	178 (65.4)
P value		0.02	0.8	0.005
Years at school				
<12	1,097 (88.5)	504 (45.9)	199 (39.5)	305 (60.5)
≥ 12	143 (11.5)	66 (46.2)	43 (65.2)	23 (34.8)
P value		1.0	0.17	0.5
Smoking (pack-years)				
Never-smoker	422 (34.0)	221 (52.4)	81 (36.7)	140 (63.3)
< 20	498 (40.2)	211 (42.4)	87 (41.2)	124 (58.8)
≥ 20	320 (25.8)	138 (43.1)	74 (53.6)	64 (46.4)
P value		0.005	0.15	0.06
Physical activity				
Active	716 (57.7)	324 (45.3)	114 (35.2)	210 (64.8)

Inactive or sedentary	524 (42.3)	246 (46.9)	128 (52.0)	118 (48.0)
P value		0.6	0.008	0.2
Binge drinking				
Yes	211 (17.0)	91 (43.1)	56 (61.5)	35 (38.5)
No	1,029 (83.0)	479 (46.6)	186 (38.8)	293 (61.2)
P value		0.6	0.9	0.8
Body mass index (kg/m^2)				
< 25	708 (57.1)	223 (31.5)	94 (42.2)	129 (57.8)
25–29.9	380 (30.6)	220 (57.9)	105 (47.7)	115 (52.3)
≥ 30	152 (12.3)	127 (83.6)	43 (33.9)	84 (66.1)
P value		<0.001	<0.001	<0.001
Years since HIV diagnosis				
<3	485 (39.1)	206 (42.5)	82 (39.8)	124 (60.2)
3-5	350 (28.3)	169 (48.3)	73 (43.2)	96 (56.8)
≥ 6	404 (32.6)	195 (48.3)	87 (44.6)	108 (55.4)
P value		0.14	0.19	0.4
Currently on HAART				
Yes	815 (65.7)	409 (50.2)	167 (40.8)	242 (59.2)
No	425 (34.3)	161 (37.9)	75 (46.6)	86 (53.4)
P value		<0.001	0.4	<0.001
CD4 count (cel/mm^3) (n=1,227)				
<350	476 (38.8)	193 (40.5)	86 (44.6)	107 (55.4)
≥ 350	751 (61.2)	372 (49.5)	153 (41.1)	219 (58.9)
P value		0.002	0.06	0.03
HIV-RNA viral load (n=1,221)				
Undetectable	713 (57.5)	280 (39.3)	124 (44.3)	156 (55.7)
Detectable	508 (42.5)	282 (55.5)	113 (40.1)	169 (59.9)
P value		<0.001	<0.001	<0.001
Total cholesterol (mg/dL) (n=1,226)				
<200	854 (69.7)	352 (41.2)	148 (42.0)	204 (58.0)
≥ 200	372 (30.3)	214 (57.5)	90 (42.1)	124 (57.9)
P value		<0.001	<0.001	0.001
HDL (mg/dL) (n=1,226)				
<35	152 (12.4)	50 (32.9)	28 (56.0)	22 (44.0)
≥ 35	1,074 (87.6) (86.7)	516 (48.0)	210 (40.7)	306 (59.3)
P value		<0.001	0.006	0.3
LDL (mg/dL) (n=1,225)				
<130	966 (78.9)	424 (43.9)	188 (44.3)	236 (55.7)
≥ 130	259 (21.1)	142 (54.8)	50 (35.2)	92 (64.8)
P value		0.002	0.04	0.1
Triglycerides (mg/dL) (n=1,227)				
<150	787 (64.1)	316 (40.2)	107 (33.9)	209 (66.1)
≥150	440 (35.9)	251 (57.0)	132 (52.6)	119 (47.4)
P value		<0.001	<0.001	<0.001
Fasting glucose (mg/dL) (n=1,226)				
<126	1,185 (96.7)	538 (45.4)	223 (41.4)	315 (58.6)
≥126	41 (3.3)	28 (68.3)	15 (53.6)	13 (46.4)
P value		0.004	0.02	0.03

Percentages for the column of total add 100%; while for prevalence rates, the 100% is obtained adding the lines

Table 1: Characteristics of HIV-infected participants and prevalence of lipohypertrophy [n (%)].

obese, patients on HAART, with CD4 counts greater than 350 cells/mm^3 and undetectable viral load were significantly associated with the presence of lipohypertrophy. Increased levels of total cholesterol, HDL and LDL fractions, triglycerides and glucose were also associated with lipohypertropy.

When gender-related differences were analyzed, physical inactivity, obesity and undetectable viral load in men continued to be associated with lipohypertropy. Among women, those with non-white skin color, obesity, on HAART, CD4 counts greater than 350 cells/mm^3 and undetectable viral load were associated with lipohypertropy.

The characteristics of the participants, classified according to the presence or absence of lipoatrophy, are shown in table 2.

With regard to lipoatrophy, 660(53.2%) had two or more signs of peripheral fat loss, and the percentage was nonsignificantly higher in men (53.8%) than in women (52.6%). Non-white skin color (60.4%)

	Total (n=1,240)	Prevalence of Lipoatrophy		
		Overall (n=1240)	Men (n=628)	Women (n=612)
Gender				
Men	628 (50.6)	338 (53.8)	-	-
Women	612 (49.4)	322 (52.6)	-	-
P value		0.7		
Age (years)				
18-34	471 (38.0)	240 (51.0)	98 (40.8)	142 (59.2)
35-49	591 (47.7)	329 (55.7)	191 (58.0)	138 (42.0)
50-78	178 (14.3)	91 (51.1)	49 (53.8)	42 (46.2)
P value		0.3	0.2	0.4
Skin color				
White	692 (55.8)	329 (47.5)	178 (54.1)	151 (45.9)
Non-white	548 (44.2)	331 (60.4)	160 (48.3)	171 (51.7)
P value		<0.001	<0.001	0.033
Years at school				
<12	1,097 (88.5)	606 (55.2)	305 (50.3)	301 (49.7)
≥ 12	143 (11.5)	54 (37.8)	33 (61.1)	21 (38.9)
P value		<0.001	<0.001	0.3
Smoking (pack-years)				
Never-smoker	422 (34.0)	202 (47.9)	86 (42.6)	116 (57.4)
<20	498 (40.2)	265 (53.2)	128 (48.3)	137 (51.7)
≥ 20	320 (25.8)	193 (60.3)	124 (64.2)	69 (35.8)
P value		0.003	0.04	0.10
Physical activity				
Active	716 (57.7)	397 (55.4)	188 (47.4)	209 (52.6)
Inactive or sedentary	524 (42.3)	263 (50.2)	150 (57.0)	113 (43.0)
P value		0.07	0.3	0.09
Binge drinking (n=1,226)				
Yes	211 (17.0)	101 (47.9)	71 (70.3)	30 (29.7)
No	1,029 (83.0)	559 (54.3)	267 (47.8)	292 (52.2)
P value		0.4	0.2	0.17
Body mass index (kg/m^2)				
<25	708 (57.1)	445 (62.9)	252 (56.6)	193 (43.4)
25–29.9	380 (30.6)	152 (40.0)	74 (48.7)	78 (51.3)
≥ 30	152 (12.3)	63 (41.4)	12 (19.0)	51 (81.0)
P value		<0.001	<0.001	0.003
Years since HIV diagnosis				
<3	485 (39.1)	234 (48.2)	113 (48.3)	121 (51.7)
3-5	350 (28.3)	174 (49.7)	88 (50.6)	86 (49.4)
≥ 6	404 (32.6)	252 (62.4)	137 (54.4)	115 (45.6)
P value		<0.001	0.002	0.02
Currently on HAART				
Yes	815 (65.7)	474 (58.2)	248 (52.3)	226 (47.7)
No	425 (34.3)	186 (43.8)	90 (48.4)	96 (51.6)

P value		<0.001	<0.001	0.002
CD4 count (cel/mm^3) (n=1,227)				
<350	476 (38.8)	265 (55.7)	148 (55.8)	117 (44.2)
≥ 350	751 (61.2)	387 (51.5)	185 (47.8)	202 (52.2)
P value		0.16	0.04	0.9
HIV-RNA viral load (n=1,221)				
Undetectable	713 (58.4)	279 (39.1)	151 (54.1)	128 (45.9)
Detectable	508 (41.6)	369 (72.6)	181 (49.1)	188 (50.9)
P value		0.3	0.3	0.7
Total cholesterol (mg/dL) (n=1,226)				
<200	854 (69.7)	465 (54.4)	242 (52.0)	223 (48.0)
≥ 200	372 (30.3)	186 (50.0)	89 (47.8)	97 (52.2)
P value		0.04	0.13	0.15
HDL (mg/dL) (n=1,226)				
<35	152 (12.4)	81 (53.3)	58 (71.6)	23 (28.4)
≥ 35	1,074 (87.6) (86.7)	570 (53.1)	273 (47.9)	297 (52.1)
P value		0.9	0.7	0.6
LDL (mg/dL) (n=1,225)				
<130	966 (78.9)	528 (54.7)	280 (53.0)	248 (47.0)
≥ 130	259 (21.1)	122 (47.1)	50 (41.0)	72 (59.0)
P value		0.03	0.19	0.09
Triglycerides (mg/dL) (n=1,227)				
<150	787 (64.1)	419 (53.2)	203 (48.4)	216 (51.6)
≥150	440 (35.9)	232 (52.7)	128 (55.2)	104 (44.8)
P value		0.9	0.10	0.15
Fasting glucose (mg/dL) (n=1,226)				
<126	1,185 (96.7)	629 (53.1)	316 (50.2)	313 (49.8)
≥126	41 (3.3)	22 (53.7)	15 (68.2)	7 (31.8)
P value		0.9	0.5	0.5

Percentages for the column of total add 100%; while for prevalence rates, the 100% is in the lines

Table 2: Characteristics of HIV-infected participants and prevalence of lipoatrophy.

and low education level (55.2%) variables were significantly associated with lipoatrophy (P value<0.001). Individuals classified as physically active, measured by the IPAQ, had higher prevalence of lipoatrophy (55.4%, P value 0.07) than the others. Smoking (P value 0.003) and BMI<25 kg/m^2 (P value<0.001) were also positively associated with the presence of lipoatrophy. In addition, HIV-infected individuals with longer diagnosis time and on HAART also had association with the presence of lipoatrophy.

Table 3 shows the association between physical activity and lipohypertropy and lipoatrophy in both men and women, adjusted for confounding factors modeled in a progressive way. Physical inactivity showed to be a risk factor for lipohypertropy only in men, being associated even after the full control for confounding factors.

Table 4 shows the association between physical activity measured by the IPAQ and mean fasting glucose and lipid levels. Metabolic parameters seem to be higher among individuals on HAART, in comparison to HAART-naive patients. Among individuals HAART-naive, physically activity had lower mean total cholesterol, LDL and fasting glucose (P value<0.03) than among insufficient active individuals, while for those on HAART, only triglycerides levels were higher among the insufficient active (P value=0.02).

Discussion

This study detected high prevalence of lipohypertrophy (46%) and lipoatrophy (53.2%) among HIV-infected individuals. These results are in accordance with prospective studies, which were confirmed with the use of Dual X-Ray Absorptiometry (DEXA), high prevalence of both conditions. Prevalence of lipodystrophy ranged from 14% to 63% [16]. There was an association between gender and lipohypertrophy, since it was more prevalent in women than in men. The findings of this study are consistent with those previously described, since women are at increased risk for central fat accumulation, whereas men have a higher risk for facial lipoatrophy [17]. However, this latter finding was not found in this study.

Lipodystrophy was also associated with non-white skin color. Even lipoatrophy has been associated with white skin color non-Whites seem to have higher central fat accumulation [18,19]. This finding

IPAQ	Lipohypertrophy		Lipoatrophy	
	Prevalence Ratio (95% CI)	P value	Prevalence Ratio (95% CI)	P value
Men Actives* Insufficient physical activity	1.0 1.31 (1.07-1.60)	0.008	1.0 0.93 (0.80-1.08)	0.3
Model 1*	1.31 (1.07-1.59)	0.008	0.93 (0.80-1.07)	0.3
Model 2**	1.30 (1.07-1.59)	0.009	0.94 (0.91-1.08)	0.4
Model 3***	1.30 (1.07-1.58)	0.01	0.94 (0.82-1.09)	0.4
Model 4****	1.30 (1.07-1.58)	0.009	0.94 (0.82-1.09)	0.4
Model 5*****	1.34 (1.10-1.63)	0.004	0.93 (0.80-1.07)	0.3
Model 6******	1.34 (1.10-1.63)	0.004	0.92 (0.80-1.07)	0.3
Women Actives* Insufficient physical activity	1.0 0.91 (0.78-1.06)	0.2	1.0 0.87 (0.74-1.03)	0.10
Model 1*	0.91 (0.78-1.06)	0.2	0.88 (0.75-1.03)	0.11
Model 2**	0.92 (0.79-1.08)	0.3	0.89 (0.76-1.04)	0.15
Model 3***	0.93 (0.79-1.08)	0.3	0.89 (0.76-1.05)	0.17
Model 4****	0.92 (0.79-1.08)	0.3	0.90 (0.76-1.06)	0.19
Model 5*****	0.93 (0.80-1.08)	0.3	0.90 (0.77-1.06)	0.2
Model 6******	0.93 (0.80-1.08)	0.3	0.91 (0.77-1.07)	0.2

*adjusted for age
**adjusted for age and race
***adjusted for age, race and education
****adjusted for age, race, education and pack years
*****adjusted for age, race, education, binge drinking and CD4
******adjusted for age, race, education, binge drinking, CD4 and HAART

Table 3: Association between physical activity and lipohypertrophy and lipoatrophy adjusted for confounding variables.

	Mean (SD)	Insufficient active	Active	P-value
	HIV patients HAART-naïve (n=425)			
Total cholesterol (mg/dL)	173.7 ± 37.5	179.6 ± 38.0	169.8 ± 36.7	0.009
HDL (mg/dL)	49.8 ± 13.1	50.3 ± 12.2	49.5 ± 13.7	0.5
LDL (mg/dL)	99.9 ± 32.7	104.6 ± 34.0	96.7 ± 31.5	0.02
Fasting glucose (mg/dL)	84.3 ± 22.3	87.3 ± 29.1	82.3 ± 16.0	0.03
Triglycerides (mg/dL)	120.6 ± 63.3	121.0 ± 59.2	120.3 ± 66.0	0.9
	HIV patients currently on HAART (n=815)			
Total cholesterol (mg/dL)	187.9 ± 45.7	189.5 ± 44.9	186.7 ± 46.4	0.4
HDL (mg/dL)	51.9 ± 14.1	51.1 ± 14.6	52.4 ± 13.7	0.2
LDL (mg/dL)	103.0 ± 38.0	102.8 ± 36.5	103.2 ± 39.1	0.9
Fasting glucose (mg/dL)	88.2 ± 29.9	88.9 ± 30.1	87.6 ± 29.8	0.5
Triglycerides (mg/dL)	167.9 ± 121.1	179.1 ± 122.2	159.4 ± 119.7	0.02

Table 4: Association between physical activity and metabolic profile among treatment-naive HIV-infected individuals or under antiretroviral therapy.

is consistent with that described in the literature [17,20,21] and may represent the presence of mixed lipodystrophy.

Lipohypertrophy was also associated with the use of HAART, CD4 count ≥ 350 cells/mm^3 and undetectable viral load. In the gender-related analysis, the association of lipohypertrophy with these clinical variables was observed in women, but remained associated only with undetectable viral load in men. Longer HIV infection and the use of HAART were also positively associated with the presence of lipoatrophy. The literature shows some evidence of the association between antiretroviral treatment and the occurrence of lipodystrophy, since the introduction of HAART [22,23]. The factors most strongly associated with lipodystrophy are the use of HAART for longer period, use of protease inhibitors and age [19,24,25]. In this study, no analysis was performed in the use of HAART by class of antiretroviral drugs, but protease inhibitors are widely used in triple therapy in patients with clinical indication for using pharmacological treatment. Non-smokers had higher prevalence of lipohypertrophy, but this was not observed in the gender-related analysis, whereas smokers were associated with the presence of lipoatrophy. A study conducted with 450 male smokers, individuals not infected with HIV, found an association between smoking and increased visceral fat accumulation [26]. In the short term, nicotine increases energy expenditure and could reduce appetite, which may explain less weight gain than nonsmokers. However, smoking increases insulin resistance and is associated with central fat accumulation [26]. Obesity was directly associated with the presence of lipohypertrophy, and normal individuals were associated with lipoatrophy. Weight, height and BMI are important variables for lipodystrophy assessment. However, these criteria alone are not sufficient to distinguish patients with abnormal fat redistribution (lipoatrophy or lipohypertrophy), since they may be within normal limits in patients with mixed lipodystrophy [2].

This study showed that lipoatrophy was observed in a greater proportion among physically active individuals, but in the gender-related analysis, there was no statistically significant difference even after adjustment for confounding variables. Lipohypertrophy in men was associated with inactivity, independently of age, skin color, education, binge drinking, CD4 and HAART. Such association was not observed among women. Few studies have analyzed the association of physical activity with HIV-lipodystrophy syndrome. A study conducted with 150 HIV-infected individuals taking Stavudine or Zidovudine concluded that physical activity is an independent protective factor for HIV-lipodystrophy syndrome, especially when combined with a proper diet [27]. Segatto et al. concluded that a physically active lifestyle has a protective effect against the occurrence of lipodystrophy related to HAART [28]. Physical activity is considered a preventive intervention for lipohypertrophy, which accounts for maintaining the body composition [29] and prevent the accumulation of central body fat [30]. However, despite the beneficial effect of exercise and/or physical activity in preventing lipohypertrophy [31], they may worsen lipoatrophy [6,12].

With regard to the lipid profile, in the whole sample, 35.5% of participants showed increased levels of triglycerides, 30% of total cholesterol, 20.9% of LDL fraction, 3.3% of fasting glucose, and 12.3% had a reduced level of HDL. There was an association between subjects with lipohypertrophy and elevated levels of total cholesterol, HDL and LDL fractions, triglycerides and fasting glucose. Among women, only elevated levels of HDL and LDL fractions were not associated with lipohypertrophy. The use of hypotriglycemic drugs showed no difference in the prevalence of lipodystrophy (data not shown).

HIV-infected individuals have shown lipid and glucose abnormalities, usually associated with the use of HAART [6,22,32,33]. In a cohort of HIV-infected individuals in Uganda, there was an increase of basal levels of total cholesterol, HDL, LDL and triglycerides 24 months after starting HAART. Triglycerides returned to basal levels at the end of the follow-up period. In this case, the increase in HDL has been described as resulting from the increase in total cholesterol [34], as observed in this study. In addition, individuals who discontinued HAART had a reduction of lipid levels, and in the resumption of treatment, there was an increase in glucose and lipid levels in only eight weeks [35,36]. Change in triglyceride levels in HIV-infected individuals is a very common finding, regardless of use of HAART [37]. However, many authors consider hypercholesterolemia and hypertriglyceridemia associated with the use of protease inhibitors [38,39].

Elevated serum triglyceride levels are associated with the occurrence of coronary heart disease [40,41]. Other changes in the lipid profile are also considered risk factors for cardiovascular disease, both in the general population and in HIV-infected individuals [7,42]. Despite the cardiovascular risk associated with the use and duration of HAART, there is evidence that chronic infection, inflammation and immune function imbalance, caused by HIV infection, contribute to changing the structure and vascular function [43,44].

Physically active HAART-naive individuals had significantly lower levels of total cholesterol, LDL fraction and glucose. Among HAART-treated subjects, physical activity was associated with lower levels of triglycerides. In adults without HIV infection, several studies have shown that exercise and physical activity have a protective effect on dyslipidemia and is associated with lower levels of total cholesterol, LDL fraction, and in particular, with lower value in serum triglyceride levels [40,45,46].

The results of this study showed higher serum cholesterol, HDL, LDL, triglycerides and glucose among insufficient active individuals. This finding may indicate that the benefits of physical activity are also applicable to HIV-infected individuals, to reduce risk factors for cardiovascular disease. However, there are limitations of the experimental design, since cross-sectional studies cannot establish cause and effect relationship. The lipid profile is influenced by intrinsic factors such as individual metabolism and family history of dyslipidemia and diabetes (genetic) [47] and extrinsic factors such as diet [48,49] and medication use [50,51].

In conclusion, the high prevalence of lipohypertrophy among HIV-infected individuals was independently associated with inactivity, and clinical and behavioral characteristics could increase the risk by 34%. Physically active HAART-naïve subjects had lower levels of total cholesterol, LDL fraction and fasting glucose levels, while those on HAART only had a significant reduction in triglyceride levels. Physical activity is a non-pharmacological strategy appropriate for the prevention or treatment of HIV lipodystrophy syndrome, whereas it has beneficial effects on lipohypertrophy and lipid levels.

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