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Lipodystrophy and metabolic syndrome in HIV-infected patients treated with antiretroviral therapy

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Abstract

Lipodystrophy (lipo) and metabolic derangements associated with an increased cardiovascular risk are observed frequently in human immunodeficiency virus (HIV)–infected patients who receive antiretroviral treatment (ART). The objective of the study was to provide detailed biochemical information about metabolic syndrome in this condition. One hundred forty-six HIV-infected male and female patients on ART for more than 6 months were compared with 156 body mass index (BMI)–matched healthy subjects. Lipodystrophy was diagnosed upon patient and physician concordance. Metabolic syndrome was defined according to the Adult Treatment Panel III criteria. Plasma adiponectin (AD) and leptin were measured by radioimmunoassay. Insulin resistance (IR) was assessed by the homeostasis model assessment (HOMA). The prevalence of metabolic syndrome was higher in HIV-infected patients on ART than in non–HIV-infected healthy controls (15.8% vs 3.2%; $P < .001$). Patients with metabolic syndrome are older (44.6 ± 6 vs 39.8 ± 8 years; $P = .004$), have an increased BMI (24.9 ± 3.8 vs 22.9 ± 9.8 kg/m^2; $P = .01$), present with a reduced AD-to-leptin ratio $\log_{10}$ (−0.19 ± 0.4 vs 0.5 ± 0.4; $P = .04$), and show increased IR (HOMA, 5.6 ± 2.7 vs 3.8 ± 2.2; $P = .001$; plasma fasting insulin, 22.9 ± 9.8 vs 16.6 ± 9.7 ng/mL; $P < .001$). In multivariate analysis, the diagnosis of lipo and HOMA were independently and significantly related to metabolic syndrome. In conclusion, the prevalence of metabolic syndrome is significantly increased in HIV-infected patients on ART and its presence is associated with lipo, increased age and BMI, IR, and a reduced plasma AD-to-leptin ratio.

1. Introduction

The metabolic syndrome (MetSynd) has been identified as a constellation of metabolic and nonmetabolic disorders in part related to defects in insulin sensitivity that lead to an increased risk for the development of cardiovascular disease (CVD) [1]. Its identification may provide additional information to the classical CVD risk factors in the clinical management of high-risk patients. A significantly increased prevalence of MetSynd in human immunodeficiency virus (HIV)–infected patients on antiretroviral therapy (ART) vs matched healthy controls has been described [2,3]. The clinical importance of this finding in terms of CVD morbidity of HIV-infected persons has not yet been adequately established. Alterations in adipocytokine balance have been proposed as the biochemical background of MetSynd [4,5], in particular variations in tumor necrosis factor α and adiponectin (AD). Moreover, reduced AD plasma levels have been proposed as a marker of MetSynd in the general population [6]. In HIV-infected patients with lipodystrophy (lipo), circulating levels of adipocytokines are altered, in particular tumor necrosis factor α, AD, and IL-6 [7,8]. Adiponectin-to-leptin ratio (A/L) has been described to be reduced in this condition, being a good predictor of insulin resistance (IR) and cardiovascular risk markers such as C-reactive protein and triglyceride (TG) levels [8]. There is very scant information about the biochemical background of MetSynd in HIV-infected patients. Aiming to provide a detailed description of this condition, we analyzed the plasma levels of AD and leptin in a cohort of HIV-infected patients on ART and correlated with metabolic parameters and the presence of diagnostic criteria for MetSynd.

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2. Methods

2.1. Patients and control group

One hundred forty-six consecutive, ambulatory, HIV-infected patients were included in the study. Written informed consent was obtained in all cases. Patients with any active opportunistic infection or neoplasm were excluded from the study. Patients on ART for more than 6 months were included in the study. All previous and ongoing antiretroviral therapy, including exposure time to specific drugs, based on cumulative months on therapy was recorded. Control group subjects were selected from a large population-based study which aimed to estimate the prevalence of MetSynd in the general population in the province of Segovia, Spain. Exclusion criteria from this group were type 1 diabetes mellitus, liver or heart failure, hospitalization due to any surgical or medical condition in the previous year, and weight loss variation of more than 5 kg in the last 6 months. Details of this study can be found elsewhere [9]. One hundred fifty-nine healthy individuals from this original group were selected on the basis of a similar BMI. The clinical characteristics of patients and controls are shown in Table 1.

2.2. Lipodystrophy definition criteria

Clinical evaluation of lipo was obtained in every case, and diagnosis was based upon the concordance between the opinion of a single clinical examiner and that of the patient. A questionnaire on fat distribution with 4 possible answers was used: no alterations, mild, moderate, and severe changes. Different body parts were examined: the face, the extremities (questioning about fat loss), and the dorsocervical and abdominal regions (sites of possible fat accumulation). Concordance between the patient's opinion and that of the clinical examiner with at least "moderate" changes within the same anatomical location was considered as diagnostic of lipo. Lipoatrophic variant was diagnosed when only fat loss changes were present and lipoaccumulation when there was only fat deposition in the abdomen or in the dorsocervical area. Finally, a mixed form was diagnosed when both fat loss and accumulation were present simultaneously in the same patient. Obese patients (BMI, >30 kg/m^2) were not included in the study. Lipo was present in 99 cases, 72.7% with fat atrophy, 26.3% with a mixed form, and 1% with lipoaccumulation.

2.3. Diagnosis of metabolic syndrome

Adult Treatment Panel III criteria [1] were used in this study, and MetSynd was diagnosed when 3 or more of the following were present: abdominal obesity (men, >102 cm; women, >88 cm), hypertriglyceridemia of 150 mg/dL or higher, low high-density lipoprotein (HDL) cholesterol (men, <40 mg/dL; women, <50 mg/dL), blood pressure (BP) of 130/85 mm Hg or higher or current use of antihypertensive medication, and fasting glucose of 100 mg/dL or higher, or previously diagnosed diabetes mellitus.

2.4. Laboratory determinations

Blood was drawn from each subject after an overnight fast on the morning of the study visit. Blood samples were immediately centrifuged at room temperature after collection. Samples were immediately frozen at −70°C until hormonal determinations were made. Plasma glucose was determined in duplicate by a glucose-oxidase method adapted to an auto analyzer. Total cholesterol (CHOL), TGs, and HDL cholesterol were determined by enzymatic methods using commercial kits (Boehringer-Manheim, Madrid, Spain). Low-density lipoprotein (LDL) cholesterol was calculated by the Friedewald method, except in patients with TG levels higher than 400 mg/dL (LDL = CHOL − ([TG/5] + HDL). CD4+ lymphocyte cell count was calculated by standard flow cytometry. Human immunodeficiency virus–1 viral load (VL) was established by standard polymerase chain reaction (Roche Amplicor Ultrasensitive, Roche, Basel, Switzerland), with a lower limit of 50 copies per milliliter. Hepatitis C virus infection was diagnosed with a positive enzyme immunoassay (EIA-3) anti–hepatitis C virus test.

Plasma insulin concentrations were determined by radioimmunoassay (RIA; Human Insulin Specific RIA Kit, Linco Research, St Louis, Mo). The sensitivity of the test was less than or equal to 2 μU/mL to 100 μL. The intra- and interassay coefficients of variation were less than 1% and 0.67% to 7.43%, respectively.

Insulin resistance was calculated according to the homeostasis model assessment ratio (HOMA-R) method from fasting glucose and insulin concentrations, according to the formula: insulin (μU/mL) × glucose (mmol/L)/22.5. Insulin resistance was defined using HOMA values higher than the 75th percentile from our healthy control group

Table 1
Patient's clinical characteristics

	HIV patients on treatment	Healthy controls	Statistical significance
N	146	159	
Metabolic syndrome (%)	15.8	3.2	<.001
Sex (M/F)	96/50	75/84	
Age (y)	40.6 (8.0)	44.6 (5.5)	<.001
Smokers (%)	67.1	34	<.001
BMI (kg/m^2)	23.2 (3.5)	22.8 (1.8)	NS
Waist diameter (cm)	84.1 (10.7)	81.2 (8.5)	.02
Systolic BP (mm Hg)	119.7 (13.5)	113.8 (13.1)	<.001
Diastolic BP (mm Hg)	73.7 (9.1)	73.6 (8.5)	NS
Cholesterol (mg/dL)	201.5 (49.9)	203.7 (33.9)	NS
HDL (mg/dL)	48.5 (14.5)	67.2 (19.2)	<.001
LDL (mg/dL)	117.9 (38)	120.7 (29)	NS
TGs (mg/dL)	226.6 (169.7)	77.7 (49.1)	<.001
Glycemia (mg/dL)	95.4 (15.0)	83.2 (19.7)	NS
Insulin (ng/mL)	17.7 (10.0)	9.8 (5.9)	<.001
Proinsulin (pmol/L)	14.6 (14.7)	7.8 (5.8)	<.001
HOMA-r	4.1 (2.4)	2.0 (1.5)	<.001
Leptin (ng/mL)	8.6 (8.0)	6.3 (4.4)	.002
AD (μg/mL)	10.5 (11.9)	10.6 (5.5)	NS
A/L ratio Ig10	0.23 (0.4)	0.27 (0.3)	<.001

NS indicates not significant.

Table 2
Differences between HIV patients on ART with and without lipo

	Lipodystrophy	No lipodystrophy	Statistical significance
N	99 (67.3%)	47 (31.9%)	
Metabolic syndrome (%)	18.2	10.6	NS
Sex (M/F)	64/35	32/15	
Age (y)	43.1 (7.5)	38.6 (7.8)	.001
Smokers (%)	71.1	65.3	NS
BMI (kg/m^2)	23.4 (2.9)	23.1 (4.0)	NS
Waist diameter (cm)	87 (8.8)	82.2 (11.5)	.03
Systolic BP (mm Hg)	125.0 (12.8)	115.1 (12.4)	<.001
Diastolic BP (mm Hg)	75.4 (8.5)	72.1 (9.3)	.03
Cholesterol (mg/dL)	204.2 (51.4)	199.3 (48.9)	NS
HDL (mg/dL)	43.7 (9.1)	52.7 (16.9)	<.001
LDL (mg/dL)	115.6 (38.9)	108.8 (37.1)	NS
TGs (mg/dL)	245.1 (182.4)	210.9 (157.6)	NS
Glycemia (mg/dL)	99.4 (15.3)	92.2 (14.1)	.004
Insulin (ng/mL)	16.8 (9.3)	18.3 (10.5)	NS
Proinsulin (pmol/L)	13.2 (9.6)	15.7 (17.4)	NS
HOMA-r	4.1 (2.3)	4.1 (2.5)	NS
Leptin (ng/dL)	4.3 (3.0)	12.1 (9.0)	<.001
AD (μg/mL)	5.4 (4.0)	13.9 (14.0)	<.001
A/L ratio Ig10	-0.8 (0.3)	0.07 (0.5)	NS
Risk practice (%)			
Parenteral	46.4	40	NS
Homosexual	35.1	32.5	NS
Heterosexual	16.5	27.5	NS
Previous AIDS-defining condition	31.9	22.9	NS
Lipodystrophy phenotype (%)		N/A	
Lipoatrophy	72.7		
Mixed	25.2		
Accumulation	2.1		
Accumulated time on ART	56.1 (28.6)	47.6 (28.0)	NS
Accumulated time on NRTI	101.5 (48.1)	89.5 (49.4)	NS
Accumulated time on NNRTI	12.0 (17.3)	13.9 (18.9)	NS
Accumulated time on PI	27.3 (18.1)	23.6 (21.7)	NS
HIV-1 viral load (Ig10)	2.1 (1.0)	2.2 (1.0)	NS
CD4 lymphocyte count (mm^3)	548.2 (315.1)	481.3 (346.2)	NS
Hepatitis C coinfection (%)	45.7	55.7	NS

NRTI indicates nucleoside reverse transcriptase inhibitors; NNRTI, non–nucleoside reverse transcriptase inhibitors; PI, protease inhibitors.

(HOMA, >3.85).

Leptin levels were determined by a highly sensitive RIA (Human Leptin RIA Kit, Linco Research), with a lower detection limit of 0.5 ng/mL to 100 μL, and inter- and intra-assay coefficients of variation were 2% to 6% and 3% to 7%, respectively.

Adiponectin was assayed by a highly specific RIA (Human Adiponectin Specific RIA Kit, Linco Research). The lower detection limit of the method was 1 ng/mL. Intra- and interassay coefficients of variation were 2% and 2.6%, respectively.

2.5. Statistical analysis

Continuous variables that did not have a normal distribution were $\log_{10}$ transformed. The Student t test or analysis of variance was used to compare continuous variables (expressed as means $\pm$ SD), whereas categorical variables were compared using the χ^2 test. Univariate and multiple linear regressions were performed according to the dependent variables. Variables shown to be significantly influenced by univariate analysis were included in a multivariate analysis. Adjusted parameter and Pearson correlation coefficient were calculated. The existence of interactions was evaluated. Bonferroni test for post hoc comparisons was used after the analysis of variance test. The null hypothesis was rejected in each statistical test when P was less than .05. Statistical analysis was performed using SPSS version 11.5 (SPSS, Chicago, Ill).

3. Results

3.1. General

Clinical characteristics and differences between groups of HIV-infected patients on treatment and healthy controls are shown in Table 1. In comparison to the control group, highly significant differences were found in HIV-infected patients among metabolic variables, particularly TG, HDL, and leptin levels. The prevalence of other cardiovascular risk factors was increased in HIV-infected patients on ART, as shown by increased IR indexes, higher systolic BP, and excessive tobacco use. Healthy controls were older than HIV-infected patients on ART (44.6 $\pm$ 5.5 vs 40.6 $\pm$ 8 years; $P < .001$). In HIV-infected patients on ART, differences between groups of patients with and without lipo are shown in Table 2.

3.2. Metabolic syndrome

In comparison with healthy controls, an increased prevalence of MetSynd in HIV-infected patients on ART was found (15.8% vs 3.2%; $P < .001$). The prevalence of MetSynd was higher in patients with lipo (18.2%) than in patients without lipo (10.6%), but this difference did not reach statistical significance. In comparison to healthy controls, patients without lipo also presented an increased frequency for MetSynd (10.6% vs 3.2%, $P = .016$). Human immunodeficiency virus–infected patients on ART with MetSynd differed from patients without it in the following variables (Table 3): reduced A/L ratio, increased age and BMI, and higher HOMA-R and fasting insulinemia. Human

Table 3
Differences between HIV patients on ART with and without MetSynd

	HIV patients with metabolic syndrome	HIV patients without metabolic syndrome	Statistical significance
A/L ratio $\log_{10}$	−0.19 (0.4)	0.5 (0.4)	.04
Age (y)	44.6 (6.4)	39.8 (8.0)	.009
BMI (kg/m^2)	24.9 (3.8)	22.9 (3.4)	.01
Insulin (ng/mL)	16.6 (9.7)	22.9 (9.8)	<.001
HIV-1 viral load $\log_{10}$	1.8 (0.4)	2.2 (1.1)	.03
HOMA	5.6 (2.7)	3.8 (2.2)	.001
Insulin resistance	78.3%	37.2%	<.001

immunodeficiency virus–1 VL was significantly lower in patients with metabolic syndrome (1.8 ± 0.4 vs 2.2 ± 1.1 $\log_{10}$, $P = .03$). CD4 lymphocyte count and accumulated time on ART and on each drug family were similar in both groups. Hypertriglyceridemia (82.6%), low HDL level (65.2%), and high BP (65.2%) were the most frequent abnormalities that lead to the diagnosis of MetSynd. A multivariate logistic regression model including MetSynd as a dependent variable was made, and both diagnosis of lipo and HOMA were independent and statistically significantly related variables (Table 4). These results were found after adjusting for age, sex, BMI, HIV VL, CD4, c-LDL, leptin, and AD.

3.3. Insulin resistance

As previously stated, IR was defined as HOMA values higher than the 75th percentile of the healthy control group, 3.85. The prevalence of IR was significantly higher in HIV-treated groups than in healthy controls (44.1% vs 6.8%; $P < .001$). Insulin resistance prevalence was significantly increased when MetSynd was present (78.3% vs 37.2%, $P < .001$), and the estimated risk for IR increased more than twice (odds ratio [OR], 2.85; 95% confidence interval [CI], 1.3-6.3). In HIV-infected patients on ART, IR was associated with significantly reduced AD (7.3 ± 7 vs 13.1 ± 14.5 pg/mL; $P = .001$) and increased leptin plasma levels (9.9 ± 7.7 vs 7.3 ± 7.7 ng/mL; $P = .007$). Patients with IR had higher BMI (24.2 ± 3.6 vs 22.4 ± 3.2 kg/m^2; $P = .003$), bigger waist circumference (87.4 ± 11 vs 81.4 ± 10 cm; $P = .011$), and increased systolic BP (123.5 ± 14.2 vs 116.9 ± 12.8 mm Hg; $P = .008$) and diastolic BP (76.8 ± 8.6 vs 71.3 ± 8.9 mm Hg; $P = .001$). Homeostasis model assessment levels significantly correlated with proinsulin plasma levels ($r = 0.58$, $P < .001$), A/L ratio $\log_{10}$ ($r = -0.46$, $P < .001$), AD ($r = -0.39$, $P < .001$), waist circumference ($r = 0.36$, $P < .001$), diastolic BP ($r = 0.30$, $P = .001$), leptin ($r = 0.28$, $P = .001$), BMI ($r = 0.27$, $P = .002$), age ($r = 0.25$, $P = .003$), and systolic BP ($r = 0.24$, $P = .007$).

Multivariate linear regression analysis was performed including IR = yes as dependent variable. When including in this analysis all HIV-infected patient study groups, a model was found with a significant overall $R^2 = 0.34$. Independent correlates for IR were male sex (OR, 4.8; 95% CI, 1.02-23.1; $P = .004$), hepatitis C virus–positive (OR, 3.6; 95% CI, 1.07-12.36J), leptin (OR, 1.2; 95% CI, 1.1-1.41; $P < .001$), age (OR, 1.1; 95% CI, 1.02-1.19; $P = .01$), CD4 (OR, 1.02; 95% CI, 1.0-1.03; $P = .04$). This model was also adjusted for AD, BMI, time on antiretroviral therapy, time on nucleoside reverse transcriptase inhibitors, non–nucleoside reverse transcriptase inhibitors, and protease inhibitors.

3.4. Adiponectin

In both HIV and non–HIV-infected subjects, MetSynd diagnosis was associated with lower AD plasma levels (6.8 ± 7.6 vs 10.9 ± 9.2 μg/mL; $P = .004$). Human immunodeficiency virus–infected patients on ART presented with similar AD levels as healthy controls. However, patients with lipo had significantly reduced AD plasma levels (5.6 ± 4.2 μg/mL), as compared to healthy control subjects (10.6 ± 5.5 μg/mL; $P < .001$). Statistically significant correlations for plasma AD levels were found with leptin ($r = 0.18$, $P = .03$) and HDL ($r = 0.30$, $P < .001$), and an inverse correlation with BMI ($r = -0.39$, $P < .001$), waist diameter ($r = -0.39$, $P < .001$), fasting insulin ($r = -0.23$, $P = .007$), HOMA ($r = -0.27$, $P = .002$), and both systolic BP ($r = -0.24$, $P = .007$) and diastolic BP ($r = -0.33$, $P < .001$). Multivariate linear regression analysis was performed including log AD as dependent variable. When including in this analysis all study groups, a model was found with a significant overall $R^2 = 0.35$. Independent correlates for AD levels were male sex ($\beta = -.48$, $P < .001$), BMI ($\beta = -.17$, $P = .03$), and insulin plasma levels ($\beta = -.17$, $P = .03$). This model was adjusted for age, waist circumference, fasting glucose, HDL, LDL, TGs, insulin, leptin, and HOMA.

3.5. Leptin

In HIV-infected subjects, leptin plasma levels were similar in both with MetSynd diagnostic criteria and without them. As compared to patients without lipo, patients with lipo showed significantly reduced leptin levels (12.1 ± 9 vs 4.3 ± 3 ng/mL; $P < .001$). Leptin levels presented a significant correlation with AD ($r = 0.18$, $P = .03$), BMI ($r = 0.21$, $P = .012$), HDL ($r = 0.20$, $P = .015$), insulin ($r = 0.29$, $P < .001$), proinsulin ($r = 0.21$, $P = .013$), and inverse with systolic BP ($r = -0.19$, $P = .02$). A multivariate linear regression analysis was performed including log leptin as dependent variable, and a model was found with an overall $R^2 = 0.49$. In this model,

Table 4
Multivariate logistic regression model for MetSynd as independent variable, after adjusting for age, sex, BMI, HIV VL, CD4, c-LDL, leptin, and AD

	OR	95% CI	P
Lipodystrophy	5.08	0.93-27.57	.059
HOMA	1.36	1.04-1.78	.023

variables with a significant independent correlation with log leptin were TGs ($\beta = -.15$, $P = .02$), male sex ($\beta = -.53$, $P < .001$), BMI ($\beta = .16$, $P = .02$), insulin ($\beta = .32$, $P < .001$), and lipo ($\beta = -.26$, $P < .001$). This model was adjusted for age, waist circumference, fasting glucose, HDL, and LDL.

4. Discussion

We have confirmed the increased prevalence of MetSynd in HIV-infected patients on ART. Because CVD is the main clinical outcome of MetSynd, there is much concern about the prognosis of this condition in HIV-infected patients, given the fact that the increased incidence of myocardial infarction is related to accumulated time on ART [10]. Hadigan et al [11] described a metabolic syndrome characterized by fat redistribution, IR, dyslipidemia, and hypertension in HIV-infected patients on ART. In this population, an exceeding risk of CVD has been confirmed when compared to healthy controls. In particular, lipoatrophic variant may represent a particular subgroup of patients with an increased CVD risk.

The etiology of MetSynd is multifactorial, and even in non–HIV-infected patients, this syndrome may not reflect a single underlying pathological process. Genetic background, HIV infection by itself, alterations in adipocytokine balance, or the effect of ART may be partially responsible for some aspects of this heterogeneous syndrome. A recently published large epidemiological study [12] has found several factors related to an increased risk for MetSynd in HIV-infected patients: increased age and BMI, lower CD4 nadir, and longer protease inhibitor exposure. Also, metabolic derangements as impaired glucose tolerance, diabetes mellitus, hypertriglyceridemia, and reduced levels of HDL are commonly observed in this population [13]. In our patient group, hypertriglyceridemia, low HDL, and high BP were the most prevalent abnormalities found, and also a significant increased prevalence of IR. This factor has been advocated as a causative factor of MetSynd in the general population [14], as well as low levels of AD, the proposed molecular link between IR, visceral adiposity, and increased CVD. There is very scant information about the biochemical background of MetSynd in HIV-infected patients. We have shown that the prevalence of IR is high and that A/L ratio is significantly reduced in HIV-infected patients on ART who present with diagnostic criteria for MetSynd. The finding of a reduced A/L ratio has been previously described in HIV-infected patients on ART [15] and may reflect an abnormal metabolic profile with an increased incidence of IR and dyslipidemia. Patients with mixed forms of lipo present with the most severe metabolic alterations, with an increased prevalence of IR and A/L ratio reduction. Probably, the main reason for this diminished ratio is the reduction in AD plasma levels that is frequently observed in patients with lipo [16]. Hypoadiponectinemia may reflect a direct toxic effect of ART on subcutaneous adipose tissue that leads to lipoatrophy and may also reflect the accumulation of visceral adipose tissue [17]. The relative contribution of leptin to the reduction in A/L ratio is unclear. We have described a reduction of plasma leptin levels in lipoatrophic patients [18] that was subsequently confirmed by other groups [19]. Moreover, a significant reduction in leptin secretion and diminished leptin pulse amplitude has been found to be significantly associated with fat loss in this population [20]. Leptin plasma levels are independently related to the absence of clinical features of lipo when on ART and IR. When the central accumulation phenotype of lipo is present, increased leptin levels may reflect an overproduction by increased fat mass. A state of leptin resistance has been suggested to be a causative factor in IR observed in obesity with secondary lipid accumulation [21]. On the other hand, a reduction in leptin plasma levels may play a role in IR, as observed in HIV-infected patients with predominant lipoatrophy [19], and in congenital forms of lipoatrophy, where leptin treatment has been shown to reverse metabolic alterations and improve insulin sensitivity [22]. A clear limitation of our study is the lack of fat distribution measurements for the whole population of patients studied. Another weakness common to many other clinical studies is the absence of an objective practical criterion for the diagnosis of lipo.

Clinical implications could be drawn from the results of this study. Both the increased prevalence of MetSynd and the very high prevalence of IR pose a risk per se in terms of CVD that should be kept in mind when planning therapeutic strategies for HIV infection and CVD prevention. Lifestyle changes aimed at obtaining an ideal weight such as increased exercise should be implemented, as well as the use of pharmacological interventions aimed at reducing LDL and high BP when indicated. The prevalence of cigarette smoking is extremely high in our patient population and must be considered as an initial step in CVD prevention. The role of insulin sensitizers is not adequately established in clinical practice but should be considered in certain cases. Both metformin [23] and rosiglitazone [24] treatment have been shown to reduce IR and improve metabolic parameters in HIV-infected patients with lipo.

In conclusion, we describe an increased prevalence of metabolic syndrome in a cohort of HIV-infected patients on ART with a 67% prevalence of lipo, when compared to BMI-matched healthy subjects. In this population, a high prevalence of IR, with a significant reduction in A/L ratio, is the more relevant biochemical finding.

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