Clinical and metabolic profile of HIV-positive patients with lipodistrophy

Perfil clínico e metabólico de pacientes soropositivos para HIV portadores de lipodistrofia

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ABSTRACT

Study Design: Descriptive Study

Objective: To evaluate the clinical and metabolic profile of HIV-seropositive patients on HAART with a diagnosis of associated lipodystrophy. **Methods:** We analyzed data computed in a protocol attached to the records of patients treated at the University Hospital of the Medical School of Ribeirão Preto. **Results:** 69.7% of the participants were male. Mean ± standard deviation body mass index was 24.7 ± 3.6 kg/m^2 and 26.7 ± 5.98 kg/m^2, and average weight 72.78 ± 12.7 kg and 65.94 ± 15.4 kg for males and females, respectively. The percentage of lean mass was greater in men (p = 0.0008) and body fat was greater in women (p = 0.0006). Median total cholesterol was 235 mg/dl and median triglycerides were 387 mg/dl. Fifty percent of the patients had abdominal lipohypertrophy, 27.9% facial lipoatrophy, and 12.5% cervical lipohypertrophy. **Conclusion:** Clinical and metabolic changes were detected, which represent additional risk factors for the occurrence of coronary diseases in these patients.

Keywords: Patients/metabolism. Lipodystrophy. Antiretroviral Therapy, Highly Active. HIV. HIV-Associated Lipodystrophy Syndrome. Cardiovascular Diseases.

Introduction

Acquired immunodeficiency syndrome (AIDS) was first detected in the 1980's after the discovery and definition of the first cases in the U.S., Haiti and Central Africa. Originally limited to specific areas, the syndrome quickly spread to various regions of the world, becoming a pandemic.[1]

According to the Joint United Nations Programme on HIV/AIDS annual report, more than 33 million people are currently living with HIV/AIDS in the world. In Brazil, 474,273 cases were notified from 1980 to June 2007.[2]

The infection natural course is characterized by intense and continuous viral replication resulting in the destruction of CD4$^+$ cells (lymphocyte cells responsi-

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Artigo recebido em 07/10/2010
Aprovado para publicação em 20/01/2011

ble for the recognition of antigens foreign to the organism) which, with other immune system changes, leads to immunodeficiency. The suppression of T4 lymphocytes or T helper cells characterizes an immunosuppressive reaction's final stage that leads the organism to be highly susceptible to the development of tumors and opportunistic infections.[3]

The first drug used for the HIV-seropositive treatment was Zidovudin, a medication originally used by patients with cancer which was able to reduce viral replication.2 Drug treatment evolved with the first protease inhibitors (PI) and the nucleoside-analogue reverse transcriptase inhibitors (NRTI) or non-nucleoside (NNRTI) development, followed by the discovery that drug combination was more effective in reducing the progression of infection. This finding led a new anti-HIV therapy proposal, the Highly Active Antiretroviral Therapy (HAART),[4] which consists of a therapeutic drugs combination, including PI class and NRTI or NNRTI.[5]

The HAART use promotes a significant viral replication suppression and reduces the opportunistic infections occurrence, thus also reducing morbidity and mortality.[6,7] However, the use of antiretroviral therapy is accompanied by severe side effects including clinical and metabolic changes such as peripheral lipoatrophy, central lipohypertrophy, body fat redistribution, dyslipidemia, insulin resistance, and changes in glucose metabolism. The set of these alterations is known as HIV lipodystrophy syndrome (HIVLS).[1,3,4]

The mechanisms responsible for metabolism and body composition's abnormalities have not been well defined.[8] These changes increase the risk of hypertriglyceridemia's complications and psychological disorders, in addition to accelerating the occurrence of atherosclerosis and cardiovascular diseases (CVD) due to HIV infection and/or antiretroviral treatment.[9,10]

The nutritional study of HIV-seropositive persons is directly related to the disease's prognosis.[11] Studies assessing the HIV-positive patients' metabolic profile at the beginning of or even during treatment are important for an appropriate diagnosis and nutritional intervention, in order to improve the life quality and life expectancy of treated subjects.

Thus, the objective of the present investigation was to assess the clinical and metabolic profile of HIV-positive patients on HAART with associated lipodystrophy diagnosis, based on personal, clinical and family history of these individuals, besides the analysis of characteristics physical HIVLS signs and the evaluation of their lipid and glycemic profile.

Methods

The study was conducted at the Special Unit for the Treatment of Infectious Diseases (UETDI), Dyslipidemia Outpatient Clinic (ADIS), of the University Hospital, Faculty of Medicine of Ribeirão Preto (HC-FMRP).

The selected study group was consisted in HIV-seropositive patients of both sexes, aged 20 years or older, attended at ADIS from January 2003 to August 2009, with different viral loads and in different disease stages, receiving HAART and with a diagnosis of dyslipidemia.

Data collection was organized based on a questionnaire regarding personal data, including lifestyle, presence of chronic non-communicable diseases (CNCD), dyslipidemia classification, HAART drug class; family history of CNCD; anthropometric data, including weight, height, abdominal circumference, skinfolds and electrical bioimpedance; physical examination to evaluate fat distribution and malnutrition signs; and lipid and glucose laboratory exams. The answers, excepted for anthropometric and laboratory data, were given as "yes", "no" or "unknown/ignored".

These data were collected at the first visit, by the professionals responsible for routine care and added to the patient's medical records. Thus, this was a retrospective study based on the collection of this information from medical records of the patient.

The lipidogram and glycemia analyses were based on the laboratory data provided by the Central Laboratory of HC-FMRP. The IV Brazilian Directive for Dyslipidemia and the Prevention of Atherosclerosis were used as reference values for the evaluation of the biochemical parameters.[12]

The project was approved by the Research Ethics Committee of HCRP and FMRP-USP on March 16, 2009 (Protocol no. 13149/2008).

Data analysis

The Epidata® software (version 3.1)13 was used to organize data for the data bank construction. The data were analyzed statistically using the StatSoft Inc.® (1996)14 and EpiData Analysis® (version 2. 2.1.171) software. The Microsoft Office Excel 2007® software was used to construct graphs and tables.

Variables were analyzed statistically using the Kruskal-Wallis test, with the level of significance set at $p < 0.05$.

Results

A total of 120 questionnaires were collected from patients attended at ADIS-HC-FMRP during the period established by research. Only one of them was discarded due to the presence of pregnancy by the time of data collection.

Most of the 119 participants were males (69.7%). Mean (± SD) age and weight differed significantly between sexes (Table 1).

Another anthropometric parameter analysis revealed an average abdominal circumference of 92.2 ± 14.69 cm for men and 92.9 ± 12.39 cm for women. Lean mass and body fat percentage differed significantly between men and women, whereas total body water percentage was similar for the two groups (Figure I).

Table 2 presents the median, minimum and maximum values of resistance, reactance, lean mass, body fat and total body water, determined by electrical bio-impedance.

Smoking, alcohol drinking and sedentary percentages detected in the study population was 19.7%, 24.3% and 63.7%, respectively.

According to previous knowledge of the patients, diabetes mellitus (DM) was present in 9.4% of them and systemic arterial hypertension (SAH) in 22.3%.

Figure 2 illustrates the distribution of CNCD among patients' relatives as reported by the patients. On average, 5.7% of them reported not know how to answer such questions (unknown/ignored) (Figure 2).

Table 3 presents the biochemical data collected. Median total cholesterol was 235 mg/dl (range: 115-889 mg/dl). Median triglyceride (TG) level was 387 mg/dl (range: 76-3278 mg/dl).

Table 1
Distribution of age, BMI and weight by sex. Data are reported as mean + SD

	Sex	N	Mean	SD	CI (95%)		P value
Age (years)	Male	81	43.12	±8.08	41.34	44.91	0.007
	Female	35	48.17	±10.61	44.53	51.82	
BMI (kg/m2)	Male	82	24.77	±3.6	23.98	25.56	0.06
	Female	34	26.79	±5.98	24.71	28.88	
Weigth (kg)	Male	83	72.78	±12.7	70.01	75.56	0.003
	Female	34	65.94	±15.4	60.57	71.31	

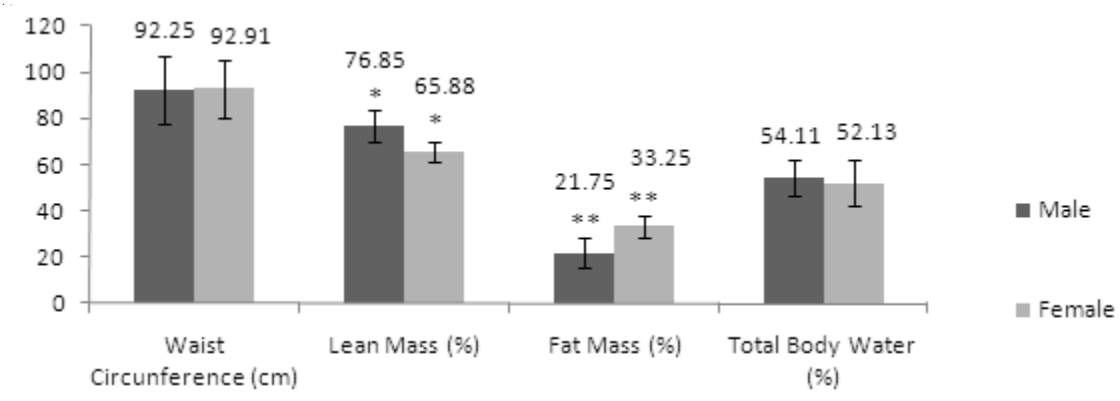

Figure 1: Mean ± SD values of waist circumference, lean mass, fat mass and total body water by sex.

Table 2
Results of bioelectrical impedance by percentile

Parameters	N	Min	p5	Median	p95	Max
Resistance	40	50	274.2	510	742.85	883
Reactance	39	39	49	61	159	426
Lean mass (%)	28	59	59	73.5	85.55	86
Fat mass (%)	28	13	13.45	24	40	40
Total body water (%)	27	27	33.4	55	68.6	73

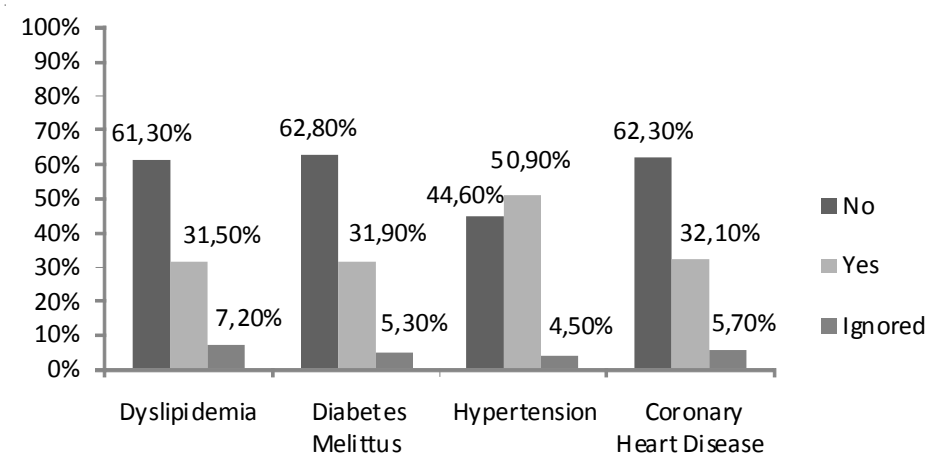

Figure 2: Family history of chronic diseases.

Table 3
Distribution of biochemical parameters by percentile

Parameters	N	Min	p5	Median	p95	Max
Total cholesterol	115	115	134.6	235	383.4	889
Triglyceride	116	76	146.85	387	1157.65	3278
LDL cholesterol	48	20	33.7	133.5	252	296
HDL-c (males)	69	18	23	35	62	79
HDL-c (females)	29	25	25	39	55	59
Glucose	72	74	81	96.5	192.65	277

Total cholesterol higher than 200 mg/dl percentage was 72.4%. 95.3% of the participants had serum TG levels above reference value (150 mg/dl), and 43.1% had glycemia levels higher than 100 mg/dl.

When the presence of hyperlipidemia or hyperglycemia was evaluated according to time of HAART use, no significant difference was detected between time of use and the parameters assessed (Figure 3).

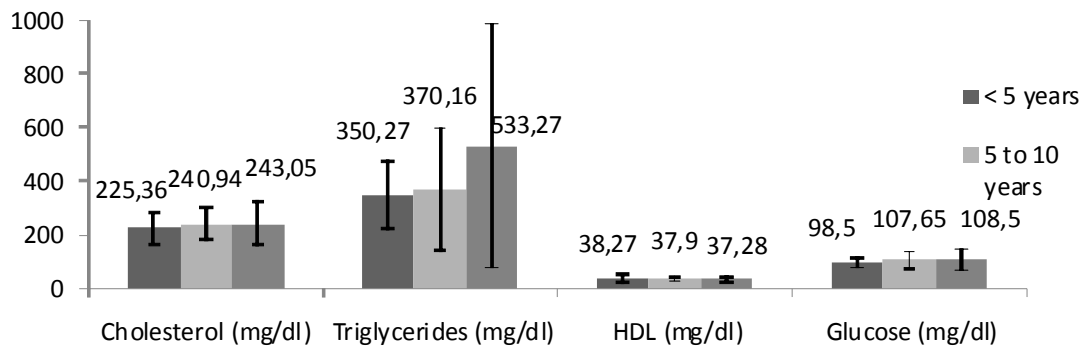

Figure 3: Distribution of biochemical parameters according to time of HAART.

Occurrence of lipodystrophy analysis demonstrated that 50% of the patients had abdominal lipohypertrophy, 27.9% had facial lipoatrophy, and 12.5% cervical lipohypertrophy.

Discussion

The present study demonstrated that most of the patients at ADIS-HC-FMRP were male with a lower average age than women (p = 0.007). Anthropometric patients' data analysis revealed that, based on body mass index (BMI), most men were eutrophic and most women overweight. Among women, average abdominal circumference was higher than reference borderline value (> 88 cm) defined for an increased risk to develop CVD.[15,16]

Bioelectrical impedance data indicated a greater lean mass percentage among males and a greater amount of body fat among women. The difference in body composition between the sexes is classically found in the general population[17] (values of total body fat between 8-24% for men and 21-35% for women are acceptable[18]). So, it is observed in this study that body composition matches with pacient's nutritional status classification.

In relation to cigarette smoking, according to the IV Brazilian Directive for Dyslipidemia and the Prevention of Atherosclerosis of the Brazilian Cardiology Society (2007),12 recent studies have reported a 17% rate of cigarette smoking people, a lower prevalence than that observed among today's patients.

Average DM prevalence detected here was within the range determined by the 1980 National Diabetes Census (from 5 to 10%), but it was above national mean (9.4% versus 7.6%). Regarding SAH, according to 1991 IBGE data,[12] the prevalence of SAH was close to, but lower than, the average for the state of São Paulo (25%). It should be pointed out that in the present study, these data weren't checked by exams, but were reported by the patients themselves, a fact that might have underestimated the real number of carriers.

High percentage of CNCD among patients' relatives suggests an increased risk of developing these diseases since the genetic component represents a risk factor for these diseases that cannot be modified.[16]

Hyperlipidemia signs and symptoms were evident among participants since this was the determinant factor for patients to be seen at the ADIS. However, very high levels of both TG and cholesterol were detected. High level of TG increases the risk of developing pancreatitis and other complications,[9] and hypercholesterolemia is directly associated with the risk of coronary disease.[19]

LDL cholesterol levels were evaluated but not analyzed, because it is known that when associated with TG levels higher than 200 mg/dl, VLDL levels are increased in a different manner and the concentration of LDL cholesterol is less related to VLDL and LDL (non-HDL) levels.[16]

Regarding glucose changes, cross-sectional studies have reported a 3-17% prevalence of symptomatic hyperglycemia among individuals treated with PI.20 In the present study, there was a 43% prevalence of glycemia levels higher than 100 mg/dl, however, the group was not analyzed according to type of antiretroviral therapy.

According to Friis-Moller (2003), patients exposed to antiretroviral therapy for a longer period of time tend to present a greater prevalence of lipodystrophy.21 Analysis of the relation between hyperlipidemia or hyperglycemia and the time of HAART did not show a significant difference, probably due to the

wide variability of the biochemical values detected during each interval. Variations detected in these biochemical results may have been due to whether or not the individuals were taking hypolipemiant and/or hypoglycemiant drugs before data collection.

In a prospective study cited by Qaqish et al (2000), women receiving HAART developed lipodystrophy within an average period of one year. Of these, 90% presented abdominal lipohypertrophy, 38% facial lipoatrophy, and 19% dorsocervical lipohypertrophy.22 In the present study, the occurrence of these three types of lipodystrophy was 50%, 27.9% and 12.5%, respectively. In both studies, such changes were detected by physical examination, although the former study also used bioelectrical impedance and anthropometric measurements, a fact that may have increased the sensitivity of the detection of these changes.

Conclusion

HIV-seropositive patients on antiretroviral treatment are at increased risk to develop CVD due to the virus itself and to the use of HAART.

The present study detected additional risk factors for coronary diseases occurrence, such as body composition, DM, SAH, hereditary influence, smoking habit, alcohol drinking, sedentary, as well as changes in the lipidogram and glycemia in these patients.

Acknowledgements

To Vassimon, Helena Siqueira, for the material and technical support and to National Counsel of Technological and Scientific Development (CNPq) for the financial support (process no: 119800/2009-8).

RESUMO

Modelo do Estudo: Estudo descritivo
Objetivo: Avaliar o perfil clínico e metabólico dos pacientes soropositivo para HIV, em uso de terapia antiretroviral fortemente ativa (Highly Active Antiretroviral Therapy - HAART) e com diagnóstico de lipodistrofia associada. **Métodos:** A pesquisa foi realizada a partir da análise de dados computados em um protocolo anexado ao prontuário de pacientes atendidos na Unidade Especial de Tratamento para Doenças Infecciosas (UETDI), no Ambulatório de Dislipidemia (ADIS) do Hospital das Clínicas da Faculdade de Medicina de Ribeirão Preto (HC-FMRP). **Resultados:** 69,7% dos participantes eram do sexo masculino. As médias (DP) de IMC foram 24,7±3.6 Kg/m^2 e 26,7 ±5.98 Kg/m^2 e média de peso 72,78±12.7 Kg e 65,94±15.4 Kg para o sexo masculino e feminino, respectivamente. A porcentagem de massa magra foi maior nos homens (p=0,0008) e de gordura corporal, maior no sexo oposto (p=0,0006). A variação do colesterol total teve mediana igual a 235mg/dl e os triglicérides, mediana de 387mg/dl. A ocorrência de lipodistrofia demonstrou que 50% dos pacientes apresentaram lipohipertrofia abdominal, 27,9% lipoatrofia facial e 12,5% lipohipertrofia cervical. **Conclusão:** Alterações clínicas e metabólicas foram encontradas, o que representa fatores de risco adicionais para a ocorrência de doenças coronarianas nestes pacientes.

Palavras-chave: Pacientes/metabolismo. Lipodistrofia. Terapia Anti-Retroviral de Alta Atividade. HIV. Síndrome de Lipodistrofia Associada ao HIV. Doenças Cardiovasculares.

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