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Dyslipidemia in Patients with Lipodystrophy in the Use of Antiretroviral Therapy

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1. Introduction

Dyslipidemia is a change in serum lipids levels, which is associated with increased risk of cardiovascular events when are found elevated (American Heart Association, 2002, Sposito et al., 2007). Before introduction of antiretroviral therapy (HAART), patients with acquired immunodeficiency syndrome (AIDS) developed a dyslipidemia characterized by isolated elevation of triglycerides (TG) and decrease in total cholesterol (TC) and its fractions (Gkrania-Klotsas & Klotsas, 2007; Mulligan, 2003). With the advent of HAART, especially with the use of protease inhibitors (PI), this situation changed to a lipid profile with elevated TG, TC, lipoproteins of very low and low density (VLDL-C and LDL-C) and decrease in high density lipoprotein (HDL-C), leaving these patients at risk for developing diabetes, hypertension and other complications (Chen et al., 2002; Furtado et al., 2007; Garg, 2000; Gkrania-Klotsas & Klotsas, 2007; Kotler, 2008; Mulligan, 2003; Sattler, 2008; Segarra-Newnham, 2002; Schering & Tovar, 2006; Yu et al., 2005).

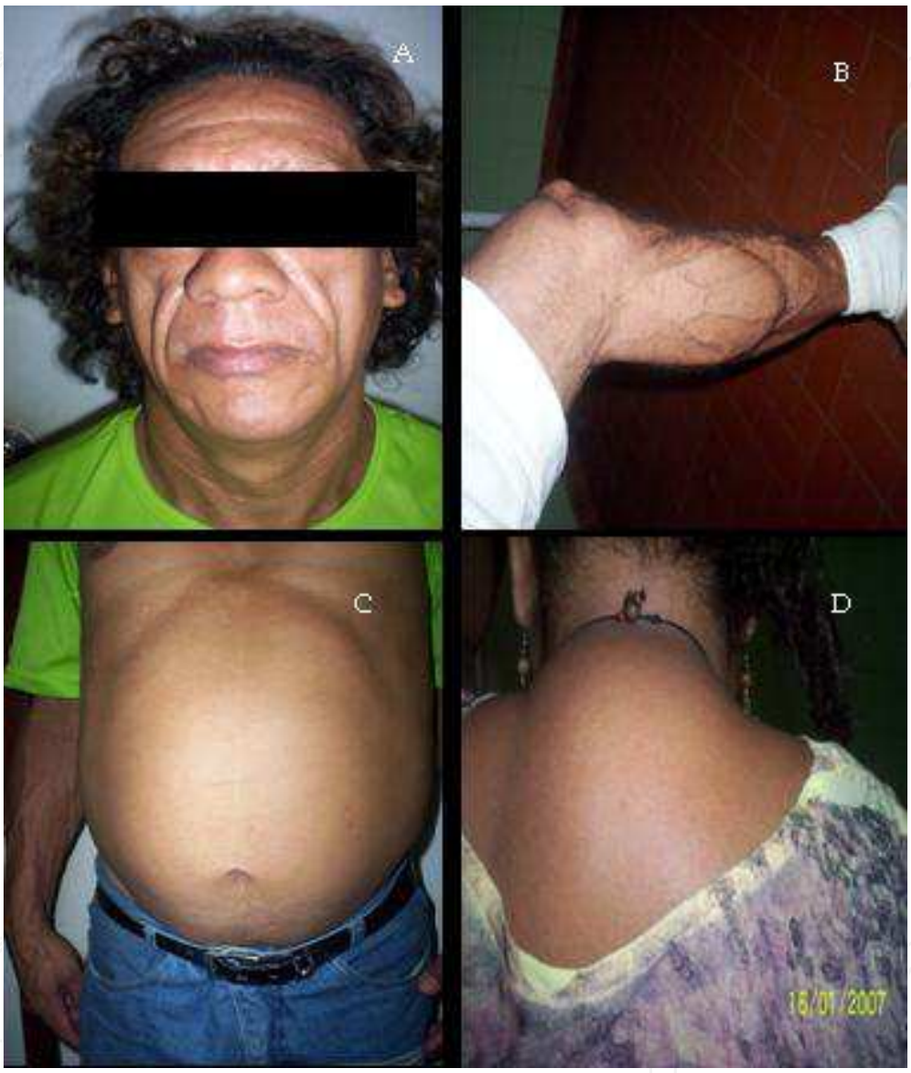
Studies estimate that the prevalence of dyslipidemia in patients with HIV (Human Immunodeficiency Virus) during use of antiretroviral therapy can vary from 33% to 82% and may be influenced by several factors including study type, sample type and time of HAART (Gkrania-Klotsas & Klotsas, 2007; Schering & Tovar, 2006; Yu et al., 2005).

2. HIV lipodystrophy syndrome

According to UNAIDS and World Health Organization (WHO) (2009) there was a large increase in the prevalence of HIV carriers in the world, reaching 33.4 million in 2008, value explained by the maintenance of annual incidence and the increase of the survival (Lihn et al. 2003; Mallewa et al., 2008). However, was noted a illness pattern change of these patients which ever left to be affected by a clinical feature characteristic of opportunistic diseases to develop HIV lipodystrophy syndrome (HIVLS) (Kramer et al., 2009; Ministry of Health of Brazil, 2008; Samaras et al., 2009; Stankov & Behrens, 2010).

Body composition abnormalities have been reported in 40-50% of HIV-positive outpatients. This proportion is higher in patients receiving antiretroviral therapy. The rate of lipodystrophy can be high depending on the characteristics of the cohort (sex, age and possibly race), the type and duration of antiretroviral therapy (Grinspoon & Carr, 2005).

The HIVLS presents three distinct forms according to distribution pattern: lipoatrophy, with fat loss in limbs, face and buttocks; lipohypertrophy, with localized increase of abdominal, breast and dorsocervical subcutaneous cellular tissue, besides visceral deposit and lipoma formation; and the mixed form with signs of both syndromes earlier (Sattler, 2008; Mello et al., 2008) (Figure 1).



Legend: A) facial lipoatrophy with facial furrows accentuated, bony prominence, and loss of Bichat's fat (malar fat). B) Lipoatrophy of the lower limbs with prominent veins. C) Visceral lipohypertrophy, with increased waist circumference and little subcutaneous tissue. D) Dorsocervical lipohypertrophy. Photos of the collection of Dr. Rosana Libonati.

Fig. 1. Morphological changes in HIV patients with lipodystrophy syndrome, Pará, Brazil.

In addition to fat distribution alterations, metabolic changes are expressed as a mixed dyslipidemia with hypertriglyceridemia, total hypercholesterolemia, low density lipoprotein (LDL-C) elevation, reduction of high density lipoprotein (HDL-C), besides the induction of insulin resistance culminating in establishment of type II diabetes (Furtado et.,

2007; Chen et al., 2002; Garg, 2000; Sattler, 2008, Yu et al., 2005). The changes in the concentrations of plasma lipids are more observed in patients receiving protease inhibitors (PI) (Yu et al., 2005).

Prospective studies investigating body composition in patients starting HAART for the first time have showed increases in fat during the initial months of treatment, followed by a progressive declining in the following three years. In one study, the decline was estimated at 14% per year in white men who received treatment regimens containing zidovudine/lamivudine or stavudine/lamivudine plus protease inhibitor or non-nucleoside reverse transcriptase inhibitor. In contrast, trunk fat increases initially and then remains stable for two or three years, resulting in relative central adiposity. These changes are clinically evident in 20 to 35% of patients after about 12 to 24 months of combination antiretroviral therapy (Grinspoon & Carr, 2005).

The type, duration and current use or not of antiretroviral therapy are strongly associated with the lipoatrophy severity. Therapy based on two nucleoside analogue reverse transcriptase inhibitors and one protease inhibitor has strong association with severe lipoatrophy (Mallon et al., 2003).

Now, the mechanism by which the protease inhibitor causes lipodystrophy remains unknown. Several protease inhibitors prevent preadipocytes differentiation and mild to moderate apoptosis in subcutaneous adipose tissue. Adipose tissue of patients with lipodystrophy has reduced expression of mRNA of several key factors involved in adipogenesis, including Sterol regulatory element binding protein (SREBP1c) and Peroxisome proliferator-activated receptor gamma (PPARγ). *In vitro* studies have shown that protease inhibitors can inhibit lipogenesis and adipocyte differentiation, stimulate lipolysis and prevent nuclear localization of SREBP-1c (Garg, 2000; Grinspoon & Carr, 2005).

The nucleoside analog more strongly associated with lipoatrophy is stavudine, particularly when used in combination with didanosine. Lipoatrophy associated with nucleoside analogue may be due in part by mitochondrial injury caused by inhibition of the mitochondrial DNA polymerase γ within adipocyte and mitochondrial DNA depletion, although the extent and specificity of this effect remains unknown. The nucleoside analogue can inhibit adipogenesis and adipocyte differentiation, promote lipolysis and exert synergistic toxic effect with protease inhibitors *in vitro* and *in vivo* (Grinspoon & Carr, 2005).

In nine studies assessing risk factors for lipoatrophy, were statistically significant more common duration and exposure to thymidine analogues, most commonly stavudine (d4T) (6/9), age (5/9), markers of disease severity (CD4/HIV RNA) (5/9), duration of therapy (3/9) and Caucasian (3/9). A prospective nonrandomized study in 40 HIV-positive patients starting antiretroviral therapy for the first time resulted after an average of 96 weeks, using multivariate analysis, that treatment with d4T is an independent factor for lipoatrophy (Lichtenstein, 2005).

In eight studies assessing lipohypertrophy, the most significant risk factors were duration of therapy (3/8), a marker of disease severity (3/8), age (3/8) and protease inhibitor use (4/8). An additional study evaluating 2258 HIV-positive patients evaluated change in adipose tissue for both gender. Logistic regression showed that men have a significantly lower adjusted risk than women have (OR: 0.47, CI 95%: from 0.38 to 0.58) and a significantly lower risk of lipohypertrophy and mixed redistribution, while the risk of lipoatrophy was similar between genders. Therefore, a rigorous multivariate analysis controlling for numerous variables reveals multiple risk factors, suggesting that the pathogenic mechanism

for fat redistribution seems to be the result of complex interactions between host, disease and drugs factors (Lichtenstein, 2005).

As for the diagnosis of HIVLS, there is not one standard pattern used to subjective body changes mentioned by the patients, anthropometric measurements and metabolic changes demonstrated in fasting laboratory tests (Diehl et al., 2008). Other tests that assist in conducting the HIVLS patients are: bone densitometry, for the investigation of osteopenia/osteoporosis; Dual-emission X-ray absorptiometry (DEXA), which allows an analysis of body composition, especially fat in the limbs, Computed Tomography, to observe presence of visceral fat deposits, and upper abdominal ultrasound for hepatic steatosis assessment (Mallon et al., 2003).

Therefore, the main consequences of HIVLS are increased cardiovascular risk and consequent development of hypertension, diabetes mellitus, atheromatous disease, stroke, myocardial infarction (Kramer et al., 2009). Psychological disorders as well as, like stress and low self-esteem by stigmatizing body changes (Santos et al., 2005; Seidl & Machado, 2008), which not cease to be risk factor for these events already mentioned by activation of sympathetic and glucocorticoids systems, and neuropeptide Y production potentiating the metabolic changes (Licht et al., 2010; Rasmusson et al., 2010).

3. Pathophysiology of dyslipidemia secondary to antiretroviral therapy

Since the implementation of antiretroviral therapy (HAART), in the 90s of last century, the treatment of AIDS has increased the mean life expectancy of HIV-infected population. Until then seen as a death sentence in a matter of short time, the disease have been faced like chronic, and with more optimism. However, despite a decrease in morbidity and mortality, HAART led to a problem that has become a major challenge that patients with AIDS must control: dyslipidemia (Cahn et al., 2010).

The dyslipidemia associated with HAART has been characteristic of elevated total cholesterol (TC), low-density lipoprotein (LDL-C) and triglycerides (TG), in addition to decreased high-density lipoprotein (HDL-C), which results in increased predisposition to the development of hypertension, insulin resistance, diabetes mellitus and cardiovascular complications. There are evidences that cardiovascular manifestations proportions in HIV-infected patients on HAART are higher than in general population (Almeida et al., 2009). This does not mean that the occurrence of dyslipidemia has emerged only with the implementation of antiretroviral drugs to treat AIDS. Before the existence of HAART had been reported lipid profile changes with high levels of triglycerides and low rate of VLDL-C and HDL-C (Sprinz et al., 2010; Grunfeld et al., 1992).

Several studies investigate ways of relating to HAART the effects of dyslipidemia like type of drug used by the patient and how the treatment regimen it has been implemented, but is still lacking a precise explanation for the lipid profile origin. Protease inhibitors (PI) are associated with dyslipidemia and insulin resistance for a considerable time, specifically ritonavir, and a variety of hypotheses (albeit not conclusive) it is presented to explain this association (Noor, 2007; Dubé et al., 2003).

One proposed mechanism to emergence of dyslipidemia is the lipoprotein lipase inhibition by PI, responsible for LDL-C increased, due to difficulty in capturing chylomicrons, resulting in lower hepatic clearance of triglycerides (Sprinz et al., 2010, as cited in Carr & Mooser, 2001). Another hypothesis is that PI has the ability to inhibit steps in lipid metabolism by binding to cellular retinoic acid binding protein type 1 (CRABP-1) and

related protein receptor LDR-c, resulting in hyperlipidemia by higher release of lipids in the circulation. More specifically, the PI on CRABP-1 receptor leads to a reduction of 9-cis retinoic acid and dimerization with the receptor activated by peroxisome proliferator-activated receptor gamma (PPAR-γ), which is involved both in apoptosis of adipocytes and in differentiation between these two. (Sprinz et al., 2010; Carr et al., 1998). A third theory, restricted to ritonavir, antiretroviral therapy suggests it increases the activity of sterol regulatory element binding protein 1 (SREBP-1c), increasing lipogenesis, the rate of VLDL-C and apolipoprotein B liver. Thus, the increase in triglycerides caused by ritonavir that could be related to elevation in hepatic lipoprotein, inhibiting degradation mediated by apolipoprotein B and SREBP-1c in liver (Riddle et al., 2001; Liang et al., 2001).

As regard the insulin resistance promoted by PI, this class of antiretroviral drugs has been related to inhibition of GLUT-4 in the transmembrane transport of glucose, leading to reduced glucose uptake mediated by insulin in peripheral tissue (skeletal muscle and adipocytes), which can lead the modification of lipid levels (Noor, 2007). The fact that some patients had a clinical and laboratory profile more or less flowered depending on the effects that PI has on the lipids metabolism may be related to genetics, suggesting that certain people are more prone to PI effects through manifestation of certain genes so far not identified (Shahmanesh et al., 2001).

With regard to nucleoside reverse transcriptase inhibitors (NRTIs), it is speculated that can lead to reduced synthesis of mitochondrial DNA, leading to decreased oxidative phosphorylation, resulting in subcutaneous adipocyte apoptosis, dyslipidemia, and increased insulin resistance (Maagaard & Kvale, 2009). The reverse transcriptase inhibitor non-nucleoside (NNRTI), particularly Efavirenz, are also related to the onset of metabolic disorders, including dyslipidemia – but they have lower participation. When compared to patients receiving Nevirapine, patients who make use of Efavirenz have higher levels of triglycerides and HDL-C (Sprinz et al., 2010, as cited in Carr et al., 1998).

The type of antiretroviral used in HAART case amends significantly the lipid profile of patient it might be replaced. However, make use of a change in medication or combination of drugs (a strategy that appears more practical than prescription of lipid, at least at first glance) does not always result in improving lipid metabolism, considering the dyslipidemia in HIV infection is related to a multifactorial framework (Sprinz et al., 2010).

Although there are doubts considering the mechanisms linked to development of dyslipidemia in patients receiving HAART, and about assumptions not fully understood, this is still the most effective treatment in patients with AIDS and should not be proscribed for patients. To minimize risks that dyslipidemia implies to health, we recommend the same precautions, both dietary and behavioral (avoiding a sedentary lifestyle) and drug (statins/fibrates) for the general population. The use of fibrates is primarily indicated for reduction of hypertriglyceridemia, while statins are used to reverse the hypercholesterolemia. However, must be careful in prescribing of statins, since there is risk of drug interactions with HAART (Sprinz et al., 2010).

4. Treatment of dyslipidemia secondary to antiretroviral therapy

Hyperlipidemia is a major risk factor for developing of atherosclerosis. Epidemiological studies in adults show a direct association between high levels of total cholesterol and LDL and the incidence of mortality and morbidity in coronary artery disease (CAD) and is LDL-C a predictor of CAD risk at any age, besides low HDL and *diabetes mellitus* (Giddings, 1999).

Dyslipidemia in HIV infection is related to a multifactorial framework (Sprinz et al., 2010), so treatment should be done with non-pharmacological and pharmacological measures.

4.1 Hypercholesterolemia

4.1.1 Non-pharmacologic therapy

The HIV-infected patients with dyslipidemia they should be screened before using those drugs as therapy, with the implementation of the change of lifestyle of these patients through diet, exercise, tobacco control, diabetes mellitus and hypertension (Dubé et al., 2003). In one study, the diet associated with exercise in 11% reduced cholesterol levels of patients infected with HIV (Henry et al., 1998). In another study showed that diet accompanied by resistance exercise at least three times a week reduced the cholesterol level by 18% and triglycerides by 25% (Jones et al., 2001).

The first measure to be taken will always be non-pharmacologic therapy, unless there is urgent need for intervention, as patients at high risk for coronary artery disease (obesity, diabetes, family history of cardiovascular disease) and extremely high levels of LDL-C greater than 220 mg / dL (Dubé et al., 2003).

4.1.2 Pharmacological therapy

The pharmacological treatment for dyslipidemia it is performed with HMG-CoA reductase inhibitors, or statins, are the main representatives of pravastatin and atorvastatin groups. They have been used extensively in clinical practice as first-line treatment for hypercholesterolemia in the general population and in HIV-infected patients, promoting reduction of cardiovascular risk in patients without no history of coronary artery disease and of progression of coronary artery stenosis with decrease of cardiovascular events recurrence, working in primary and secondary, respectively (Dube et al., 2003).

In one study, patients with altered levels of total cholesterol (TC) and triglycerides (TG), using pravastatin 20 mg/day occurring 19% decrease in the level of TC and 37% in the level of TG (Baldini et al., 2000). In another study, diet was associated with therapy with pravastatin 40 mg/day in patients with TC levels greater than 240 mg/dL, indicating a 17% decline in the levels of TC and 19% in the level of LDL-C (Moyle, 2001). Therefore, Palacios et al., in 2002, analyzing a group of patients with TC levels greater than 240 mg/dL under atorvastatin 10 mg/day was found a 27% decrease in the level of TC, 41% of TG and 37% in the LDL-C.

Thus, statins are the first choice in the treatment of elevated LDL-C (> 220 mg / dL) and patients with high total cholesterol associated with hypertriglyceridemia (TG between 200 to 500 mg/dL), initial dose may be used 20-40 mg of pravastatin or atorvastatin 10 mg monitoring possible liver toxicity with laboratory tests (Dube et al., 2003). Protease inhibitors and non-nucleoside inhibitors of reverse transcriptase enzyme use in its metabolism the cytochrome P450 pathway (Smith et al., 2001), the same route used by simvastatin, lovastatin and atorvastatin, then the first two are proscribed to patients under antiretroviral therapy and the latter can be used with caution.

Fibrates are used as second choice in the treatment of hypercholesterolemia. In patients with normal TG and elevated LDL-C levels, a slight decrease in LDL-C ranging from 5 to 20% in the studies carried out. Therefore, the therapeutic fibrates use should be reserved for treatment of hypertriglyceridemia (TG> 500 mg/dL) in these patients (Dube et al., 2003).

4.2 Hypertriglyceridemia

4.2.1 Non-pharmacologic therapy

The non-pharmacologic therapy should be first applied to all patients with hypertriglyceridemia, through modification of lifestyle; diet should be instituted to reduce fat intake, weight reduction, reduction or elimination of alcohol intake, smoking cessation control of hyperglycemia and diabetes with insulin sensitizers such as metformin. In studies, it has been found that diets associated with exercise and resistance training promotes decrease of 21% and 27%, respectively, TG levels in HIV-infected patients (Henry et al., 1998; Yarashesky et al., 2001).

Patients who demonstrate extreme elevations in TG level (> 1000 mg / dL) and with a history of pancreatitis should be treated associating pharmacologic and non-pharmacologic therapy (Dube et al., 2003).

4.2.2 Pharmacologic therapy

Drug therapy should be instituted in all patients with TG levels greater than 500 mg/dL with the introduction of Gemfibrozil with starting dose of 600 mg half an hour before meals (lunch and dinner) or fibrates at a dose 54 to 160 mg/day (Dube et al., 2003). In a study carried out in patients with TG levels higher than 400 mg/dL using fibrate dose of 200 mg/day was observed 14% and 54% decrease of TC and TG levels, respectively (Palácios et al., 2002). Therefore, in another study, patients with TG levels higher than 266 mg/dL, using Gemfibrozil 600 mg/day associated with diet, evolved with a reduction of TG values in 18% (Miller et al., 2002).

The use of statins in general is not recommended for the treatment of hypertriglyceridemia (TG> 500 mg / dL) alone, is recommended when triglyceride levels are between 200 to 500 mg/dL associated with increased total cholesterol (Dubé et al., 2003).

5. Experience of the assistance service of metabolic diseases secondary to antiretroviral therapy for patients with dyslipidemia

Assistance Service of Metabolic Diseases Secondary to Antiretroviral Therapy (HAART) of the João de Barros Barreto University Hospital (HUJBB), Brazilian national reference in transmissible infectious diseases and AIDS, actually, assist about 99 HIV carriers' patients with lipodystrophy syndrome. Into this service, the authors develop a Project titled Lipodystrophy and Antiretroviral Therapy, financed by The State of Pará Research Foundation (FAPESPA), Research Program for the Unified Health System (PPSUS). One of the Project's purposes was the implantation of the lipodystrophy ambulatory care.

The HUJBB lipodystrophy ambulatory care works with team composed by an endocrinologist, a nutrition doctoral student, two medicine M.Sc students, four medical undergraduate students. The medical accompaniment is performed once a week. In the first service is diagnosed the clinical form of lipodystrophy and requested the proper tests (total cholesterol, HDL, LDL, triglycerides, fasting glucose test, oral glucose tolerance, insulin, abdominal ultrasonography to hepatic steatosis diagnostic and computed tomography for evaluation of visceral lipohypertrophy and electrocardiogram). The first patient's return is around 45 days and subsequently every three months for medical accompaniment. Each medical consultation is also performed medical history, measurement of blood pressure, heart auscultation, anthropometric evaluation (measurements of weight, height, skin folds) and bioimpedance. In addition, if need be the patient is referred to other professionals of the multidisciplinary team HUJBB.

Of the accompanied patients with lipodystrophy syndrome in this ambulatory care, 77% (n = 77) have dyslipidemia and presents the following profile: 67.9% were male, mean age of 44.5 years, average time of HIV infection of 8, 3 years, average time of use of antiretroviral therapy for 6.9 years and body mass index of 24.5 kg/m². Regarding risk factors, it is observed that 18.2% are smokers, 40.3% alcoholics, 71.4% sedentary and 45.5% had hepatic steatosis. Regarding the classification of nutritional status (WHO, 1995) 58.4% are eutrophic, thin 6.5% and 35.1% overweight/obesity. Among the co morbidities studied, it appears that 24.7% and 21.1% are hypertensive and diabetics, respectively. When stratifying the lipodystrophy syndrome, according to the clinical manifestations, 35.1%, 10.4% and 54.5% of patients had lipoatrophy, hypertrophy and mixed syndrome, respectively. Concerning average serum lipid levels, there is high levels blood of cholesterol and triglycerides, low HDL-C, and LDL-C within the normal range. In regard to dyslipidemia classification (Sposito et al., 2007), have been observed that 48.7% of patients have mixed hyperlipidemia, 32.9% hypertriglyceridemia, low HDL-C 10.5% and 7.9% isolated hypercholesterolemia (Table 1 and 2). In the assessment of cardiovascular risk by Framingham Risk Score was found that more than 30% of the sample had medium and high cardiovascular risk.

Variables	Total Sample	n	%
Male		52	67.5
Female		25	32.5
Smoking	77	14	18.2
Alcoholism	77	31	40.3
Sedentary	77	55	71.4
Diabetes mellitus	77	17	21.1
SH *	77	19	24.7
Family history			
Diabetes	77	37	48.1
Hypertension	77	55	71.4
Dyslipidemia	72	28	38.9
Hepatic steatosis	66	30	45.5
Nutritional status**	76		
Thinness**		05	6.6
Eutrophic		44	57.9
Overweight/Obesity		27	35.5
Lipodystrophy	77		
Lipoatrophy		27	35.1
Hypertrophy		8	10.4
Mixed		42	54.5
Classification of dyslipidemia***	76		
Mixed Hyperlipidemia		37	48.7
Hypertriglyceridemia		25	32.9
Low HDL		8	10.5
Isolated hypercholesterolemia		6	7.9

Legend: SH - systemic hypertension; ** WHO, 1995; *** Sposito et al., 2007

Table 1. Patients profile with lipodystrophy and dyslipidemia accompanied by the Assistance Service of Metabolic Diseases Secondary to Antiretroviral Therapy, João de Barros Barreto University Hospital, Pará, Brazil.

Variable	Total Sample	Mean ± SD	Median
Age (years)	77	44.5 ± 9.6	45.0
ART Time (years)	77	6.9 ± 4.1	7.0
Time of HIV (years)	77	8.3 ± 5.4	8.0
BMI (kg/m²)	76	24.5 ± 4.2	23.9
Fasting glucose (mg/dL)	72	103.4 ± 27.7	98.5
Total Cholesterol (mg/dL)	76	218.9 ± 59.7	220.0
Triglycerides (mg/dL)	76	373.3± 393.8	280.5
HDL-c (mg/dL)	60	40.8 ± 13.34	39
Male HDL-c	36	37.4 ± 11.7	37.0
Female HDL-c	24	46.0 ±14.2	46.5
LDL-c (mg/dL)	58	115.6 ± 45.4	117.9

Legend: ART – Antiretroviral Therapy, BMI – body mass index, SD standard deviation.

Table 2. Distribution of mean and median values of some variables in patients with lipodystrophy and dyslipidemia accompanied by the Assistance Service of Metabolic Diseases Secondary to Antiretroviral Therapy, João de Barros Barreto University Hospital, Pará, Brazil.

The ambulatory care authors conducted an intervention study with outpatient HIV-positive with lipodystrophy syndrome, in use of HAART in the period October 2006 to December 2007. Patients were evaluated every quarter for four visits. This study followed all the guidelines contained in Resolution 196/1996 of the National Committee for Ethics in Research (CONEP), being approved by the Ethics in Human Research of the Center for Tropical Medicine, Federal University of Para, according to opinion of approval No. 058/2006, to date of October 19, 2006. The sample consisted of patients with positive serology for HIV, use of HAART for at least 12 months, with clinical diagnosis of lipodystrophy. We selected only adult patients, aged 20 to 60 years, of both sexes. All were invited and agreed to participate by reading and signing the Free and Informed Consent Term - FICT.

We excluded all patients with mental illness, malignant tumors, and chronic users of glucocorticoids, Diabetes Mellitus and dyslipidemia diagnosed before starting HAART and those who did not achieve at least three follow-up visits clinical and nutritional care at the Ambulatory care of Lipodystrophy HUJBB.

To collect data we used a treatment protocol for metabolic evaluation, nutritional counseling and patient outcomes, among several details registered there were: patient identification, socio-economic, personal and family morbidity history, time of HIV diagnosis, time of HAART treatment, clinical history and biochemical tests. Among the lipodystrophy syndrome metabolic changes were required tests to total serum cholesterol, LDL-C, HDL-C and triglycerides for dyslipidemia analysis (Sposito et al., 2007).

We studied 29 patients, 17 (59%) and 12 (41%), male and females, respectively, with an average age of 46.07 (± 9.04) years. In males, the average age was 47.59 (± 7.66) years, median 46 years, whereas in females the mean age was 43.92 (± 10.67) years, median 44. The most prevalent age group for both sexes was 41 to 50 years.

In regarding to lipodystrophy syndrome classification, was observed that 11 (37.91%), 2 (6,9%) and 16 (55,17%) patients demonstrated lipoatrophy, lipohypertrophy and mixed syndrome, respectively. There is no sex association with lipoatrophy and mixed syndrome (p= 0.4138, OR= 0.3750, IC 95%= 0.0744 – 1.8891), whilst lipohypertrophy syndrome had predominance in females. It is assumed when calculating Odds Ratio to lipohypertrophy presence, was noted that female chance present lipohypertrophy is 2.66 times more, However, the results have not been significant (p=0.4130, IC 95% 0.5294 a 13.4334), data shown in Figure 2.

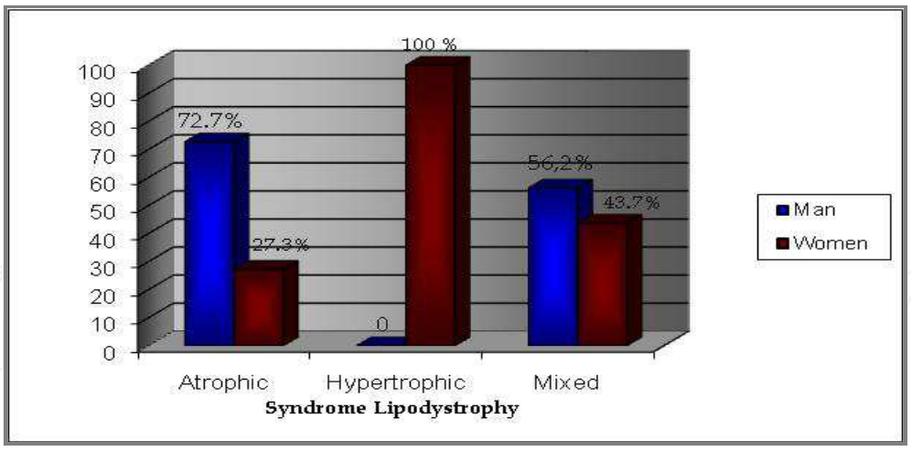
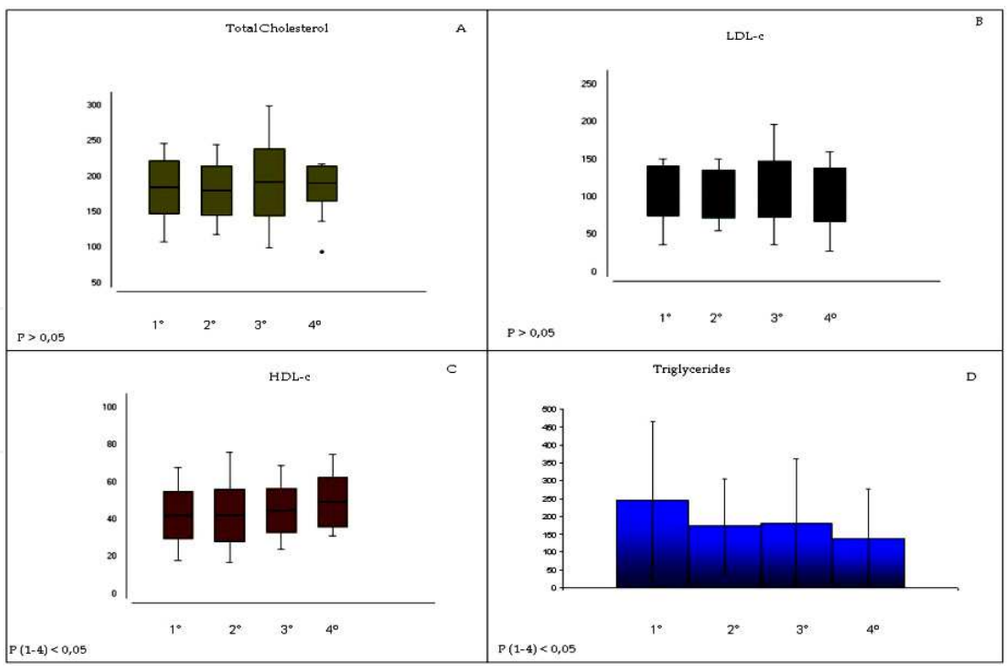


Fig. 2. Distribution of the lipodystrophy syndrome in relation to sex, Pará, Brazil 2006-2008.

The HAART temporal analysis showed that there was a growing evolution of lipoatrophy and lipohypertrophy presence in association with prolonged use of HAART (p = 0.0485, p = 0.0393, respectively).

Among the 29 patients, 6 were taking hypolipidemic. The lipid profile found in patient's evaluation, including those who had made use hypolipidemic therapy, was no statistically significant changes on the total cholesterol and LDL-C, however, for the HDL-C and triglycerides had significant differences between the first and last clinical follow-up nutritional (Figure 3).



Legend: (A) Total cholesterol, (B) LDL-C, (C) and HDL-C (D) triglycerides, distributed by quarters. Dependent t-test for paired samples.

Fig. 3. HIV patients Serum lipids who did not use hypolipidemic, distributed by quarters, 2006-2008 Para-Brazil.

When analyzing only the sample of patients who were taking hypolipidemic (n = 7), there was no statistically significant changes in the levels of serum total cholesterol, LDL-C and triglycerides (Table 3).

Biochemical Tests	**1º**	**2º**	**3º**	**4º**	**p value***
Cholesterol Total	207.7 (±40.2)	264.0 (±128.2)	216.7 (± 69.2)	219.3 (±60.9)	0.6626
LDL cholesterol	91.7 (±45.6)	136.6 (±56.3)	108.8 (±29.6)	89.7 (±46.04)	0.2539
Triglycerides	597.0 (±300.1)	996.0 (±1300.0)	488.3 (±637.6)	415.0 (±209.3)	0.0503

* Legend: *Friedman* test.

Table 3. Comparison of mean only of lipid profile of patients who were taking hypolipidemic therapy for the clinical follow-up of four nutritional consultations, Pará, Brazil 2006-2008.

In assessing relation between lipids and lipodystrophy syndrome, there was no significant association, as sample data in Table 4.

Lipodystrophy Syndrome				
	Lipoatrophy N (%)	**Lipohypertrophy N (%)**	**Mixed N (%)**	**p value**
Total Cholesterol				
Normal levels	3 (27.27)	0 (0.00)	7 (43.75)	0.3840
Abnormal levels	8 (72.73)	2 (100.00)	9 (56.25)	
LDL cholesterol				
Normal levels	9 (81.82)	1 (50.00)	14 (87.50)	0.4141
Abnormal levels	2 (18.18)	1 (50.00)	2 (12.50)	
HDL cholesterol				
Normal levels	1 (9.09)	0 (0.00)	5 (31.25)	0.2849
Abnormal levels	10 (90.91)	2 (100.00)	11 (68.75)	
Triglycerides				
Normal levels	3 (27.27)	1 (50.00)	5 (31.25)	0.3023
Abnormal levels	8 (72.73)	1 (50.00)	11 (68.75)	

Legend: N - number of patients. Test: Partitioning Chi-square.

Table 4. Association between lipid profile and lipodystrophy syndrome, Pará, Brazil 2006-2008.

In assessing comparison of mean of lipid profile of all patients before and after the clinical and nutritional intervention (first and fourth visit), there was a significant difference between the levels of total cholesterol, LDL-C, HDL-C and triglycerides between the lipoatrophy and mixed syndrome (p> 0.05) (Table 5). No analysis was performed on the lipohypertrophy syndrome due to be there of only two patients.

	Before			**After**		
	Lipoatrophy	**Mixed**	**p-value**	**Lipoatrophy**	**Mixed**	**p-value**
Total cholesterol	196.91 (±35.05)	183.00 (±41.84)	0.3744	198.14 (± 39.26)	185.58 (±45.97)	0.5538
LDL cholesterol	112.42 (±40.61)	94.54 (±34.67)	0.2308	110.37 (±50.44)	86.33 (±32.10)	0.2313
HDL cholesterol	37.91 (±11.65)	40.28 (±15.92)	0.6809	42.14 (±9.25)	44.92 (±14.64)	0.4504
Triglycerides	299.36 (±27.77)	310.75 (±259.21)	0.9133	220.86 (±193.46)	218.90 (±179.92)	0.9829

Table 5. Comparison of mean of lipid profile of all patients, including who were taking hypolipidemic therapy before and after the intervention in lipodystrophy syndrome, Pará, Brazil 2006-2008.

The manifestation of lipodystrophy syndrome with regard to gender did not present significant differences for lipoatrophy or mixed syndrome. However, the syndrome was related to female lipohypertrophy corroborating other studies (Galli et al., 2002; Heath et al., 2002) and disagreeing with most published data has been shown increased risk of lipoatrophy syndrome among women. Tien et al. (2003) in prospective study of lipodystrophy syndrome risk among HIV-infected women and non-infected observed a risk 2,1 times more of develop lipoatrophy in infected women with virus than non-infected, whereas it did not differ lipohypertrophy syndrome between the two groups and the most prevalent de form lipodystrophy was mixed syndrome (81%). Van Griensven et al. (2007) evaluated the lipodystrophy syndrome prevalence among patients using stavudine in antiretroviral therapy and found lipoatrophy syndrome prevalence in 9.8% of patients on stavudine and 4.9% with lipohypertrophy syndrome. The HAART temporal analysis showed that there was a growing evolution of the appearance of lipoatrophy and lipohypertrophy associated with HAART prolonged use, as demonstrated by studies of Lichtenstein et al. (2005) and Goujard et al. (2003).

As regards the evaluation of metabolic changes associated with use of HAART coupled with the treatment of nutritional guidance, it must be pointed out that some factors may have affected the outcome of this work as the low adherence to medical treatment, nutrition, failure to follow the previous recommendations for achieving of biochemical tests and the small sample size of patients available for this study. This difficulty in adhering to medical treatment and/or diet therapy was also found by other authors (Quintaes & Garcia, 1999; Ceccato et al. 2004; Parenti et al., 2005; Barros et al. 2007; Chencinski & Garcia, 2006). The reluctance of patients to nutritional treatment may be related to low purchasing power (Barros et al., 2007), cultural and dietary habits proper to the Amazon region, who abuse food that are rich in lipids. In addition to psychosocial factors of patients, where the prejudice, social isolation and emotional disorders such as anxiety and depression

commonly observed in patients infected with HIV make it difficult to change lifestyle (personal and food) as suggested by Quintaes & Garcia (1999) Chencinski & Garcia (2006).

There was also that patients profile evaluated before intervention reflected increase in serum total cholesterol and triglycerides, and lowering HDL-C as described in the literature (Caar et al. 1998; Hadigan et al. 2006; Having Hofstede et al., 2003; Abreu et al., 2006), disagreeing with main studies analyzed only about LDL-C, where most patients remained within normal range. Lipid disorders and association with lipodystrophy syndrome were common in all patients, especially in mixed syndrome, according to studies by Thiebaut et al. (2000) and Haugaard et al. (2005).

The lipid abnormalities evolution in patients after clinical and nutritional intervention during study noted significant changes of lowering triglycerides and increase in HDL-C, regardless of hypolipidemic use. The increased levels of HDL-C have been associated with decreased cardiovascular risk, as has been discussed in the work of Manninen et al. (1988). Where was reported that for every 1% increase in HDL-C was 3% reduction in coronary events and Pedersen et al. (1998) who said that for each 1% increase in HDL-C there was 1% reduction in coronary events, both independently of changes in LDL-C levels.

The lipid profile of patients before and after nutritional intervention clinically observed that patients who had shown serum levels of triglycerides, total cholesterol and fractions (LDL-C and HDL-C) normal at first, had increasing them at the end of treatment. These patients had borderline values facilitating risk of increased total cholesterol, LDL-C and triglycerides and decreased HDL-C associated with nutrition acceptance less than 75%. Other patients in the first consultation showed values above the reference levels for total cholesterol, LDL-C and triglycerides as well as lowering HDL-C, reaching normal values due to good acceptance to nutritional care. The remaining patients showed levels of total cholesterol, LDL-C fractions, HDL-C and triglycerides changed during the research; probably was not able to perceive the importance of nutritional treatment. There were also cases of patients who had their lipid profile within the normal range, suggesting that not only the use of HAART interfered with these metabolic changes, but also other factors may be implicated as genetic predisposition.

In regarding to lipodystrophy syndrome, the cholesterol and LDL-C means demonstrated it more significant in lipoatrophy than mixed syndrome compared before and after intervention. Triglyceride levels showed independent growing in despite to lipodystrophy syndrome, while HDL-C showed changed levels in mixed syndrome.

The physiopathology by which HAART determines HIV lipodystrophy syndrome, dyslipidemia therefore remains unknown. Second Andrade & Hutz (2002), the lipid serum levels are multifactorial characteristics, determinate by genetic and environmental factors, highlighting the genetic variability found in those genes that can affect the response to drugs used in hyperlipidemia treatment.

The authors of the lipodystrophy ambulatory care are developing a research paper about a case-control study conducted from December 2009 to July 2012. For data collection is being performed a clinical, epidemiological and nutritional evaluation where are registered information about patient identification, socio-economic conditions, personal and family history of morbidity, time of HIV diagnosis, HAART treatment duration, medication used - HAART, viral load, CD4 counts, clinical history, biochemical tests for dyslipidemia classification, anthropometric analysis and, APOAI and APOAV apolipoprotein polymorphism evaluation. This study aims to investigate these polymorphisms in an attempt to discover the main causes responsible for this metabolic disorder, the dyslipidemia.

6. Conclusion

The HAART has as one of its major collateral effect the lipodystrophy syndrome. There is necessity of more studies to deep into physiopathology of this syndrome; and metabolic and cardiovascular complications secondary to HAART. Dyslipidemia stands out as one of the most prevalent metabolic changes in patients with HIV, what makes it essential to feasibility of research in therapeutic care to clarifying of the clinical management. It is noted that nutritional guideline and/or hypolipidemic use, when have there been acceptance to treatment, takes place improvements of the lipid profile, can also there be normalization of those levels, in particular of the triglyceride levels. However, the adherence neither always takes place, what difficult the management of those patients.

7. References

Abreu, L., Escosteguy, C., Sodré, C., Godomiczer, A., Passoni, L., & Menezes, J. (2006). Tratamento anti-retroviral e hipercolesterolemia em população HIV positiva. *Revista da Sociedade de Cardiologia do Estado do Rio de Janeiro*, Vol. 19, No. 3, (Mai-Jun 2006), pp. (219-24), ISSN 2177-6024.

Almeida, L., Giudici, K., & Jaime, P. (2009). Consumo alimentar e dislipidemia decorrente da terapia antirretroviral combinada para infecção pelo HIV: uma revisão sistemática. *Arquivos Brasileiros de Endocrinologia & Metabologia*, Vol. 53, No. 5, (Jul 2009), pp. (519-527), ISSN 0004-2730.

American Heart Association. (2002). Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) Final Report. *Circulation*, Vol. 106, No. 25, (Dec 2002), pp. (3143-3421), ISSN 0009-7322.

Andrade, F., & Hutz, M. (2002). O componente genético da determinação dos lipídeos séricos. *Ciência & Saúde Coletiva*, Vol. 7, No. 1, (2002), pp. (175-182), ISSN 1413-8123.

Aouizerat, B., Kulkarni, M., Heilbron, D., Drown, D., Raskin, S., Pullinger, C., Malloy, M., & Kane, J. (2003). Genetic analysis of a polymorphism in the human apoA-V gene: effect on plasma lipids. *Journal of Lipid Research*, Vol. 44, No. 6, (Jun 2003), pp. (1167–1173), ISSN 1539-7262.

Assmann, G., Schmitz, G., Funke, H., & von Eckardstein, A. (1990) Apolipoprotein A-I and HDL deficiency. *Current Opinion in Lipidology*, Vol. 1, No. 1, (1990), pp. (110-115), ISSN: 0957-9672.

Baldini F, Di Giambenedetto S, Cingolani A, Murri R, Ammassari A, De Luca A (2000). Efficacy and tolerability of pravastatin for the treatment of HIV-1 protease inhibitor–associated hyperlipidaemia: a pilot study. *AIDS*, Vol. 14, No 11, (Jul 2000), pp. (1660–1662), ISSN: 0269-937.

Barros, E., Araujo, A., Freitas, M., & Liberato, E. (2007). Influencia da alimentação na lipodistrofia em portadores de HIV-Aids praticantes de atividade física regular. *Revista Brasileira de Prescrição e Fisiologia do Exercício*, Vol. 1, No. 2, (Mar-Abr 2007), pp. (13-18), ISSN 1981-9900.

Boccara, F., Auclair, M., Cohen, A., Lefèvre, C., Prot, M., Bastard, J.P., Capeau, J., & Caron-Debarle, M. (2010). HIV protease inhibitors activate the adipocyte renin angiotensin system. *Antiviral Therapy*, Vol. 15, No. 3, (2010), pp. (363-375).

Blanco Vaca, F., Ordóñez Llanos, J., Pérez Pérez, a., Sánchez Quesada, j. L., & Wägner Fahlin A. (2000). Lípidos, lipoproteínas y apolipoproteínas. Nuevas indicaciones en el diagnóstico, evaluación y prevención del riesgo cardiovascular. Roche Diagnóstica. S. L. In: Diaz, J. I.S. (2007). Guia practica. Marcadores Bioquimicos Cardiacos. Prologo, indice y presentacion. Acesso em 20 jun 2011. Disponível em: http://www.portalesmedicos.com/publicaciones/articles/828/2/Marcadores-cardiacos.-Factores-de-riesgo-cardiaco-en-la-aterosclerosis.-Recopilacion-de-datos-de-revisiones-bibliograficas-y-conclusiones

Caar, A., Sâmaras, K., Burton, S., Law, M., Freund, J., Chisholm, D., & Cooper, D. (1998). A syndrome of peripheral lipodystrophy, hyperlipidaemia and insulin resistance in patients receiving HIV protease inhibitors. *AIDS*, Vol. 12, No. 7, (Mai 1998), pp.51-58, ISSN: 0269-937.

Cahn, P., Leite, O., Rosales, A., Cabello, R., Alvarez, C., Seas, C., Carcamo, C., Cure-Bolt, N., L'Italien, G., Masntilla, P., Deibis, L., Zala, C., & Suffert, T. (2010). Metabolic profile and cardiovascular risk factors among Latin American HIV-infected patients receiving HAART . *Brazilian Journal of Infectious Diseases*, Vol. 14, No. 2, (Mar-Abr 2010), pp. (158-166), ISSN 1413-8670.

Carr, A., & Cooper, D. (2000). Adverse effects of antiretroviral therapy. *The Lancet*, Vol.356, No. 9232, (Oct 2000), pp. (1423-1430), INSS 0140-6736.

Ceccato, M., Acurcio, F., Bonolo, P., Rocha, G., & Guimarães, M. (2004). Compreensão de informações relativas ao tratamento anti-retroviral entre indivíduos infectados pelo HIV. *Caderno de Saúde Pública*, Vol. 20, No. 5, (Set-Out 2004), pp. (1388-1397), ISSN 0102-311X.

Chen, D., Misra, A., & Garg, A. (2002). Lipodystrophy in Human Immunodeficiency Virus-Infected Patients. *The Journal of Clinical Endocrinology & Metabolism*, Vol. 87, No. 11, (Nov 2002), pp. (4845-4856).

Chencinski, J., & Garcia, V. (Abr-Jun 2006). Dislipidemia em pacientes HIV/AIDS. In: Conselho Regional de Nutrição-3 Notícias. n.82, Acesso em 10 Mar 2008. Disponível em: <http://www.crn3.org.br/atualidades/revistas/arquivos/edicao_082_atualidades.pdf>.

Coté, H. (2007). Mechanisms of antiretroviral therapy-induced mitochondrial dysfunction. *Current Opinion in HIV and AIDS*, Vol. 2, No. 4, (Jul 2007), pp. (253-260), ISSN 1746-630X.

Diehl, L., Dias, J., Paes, A., Thomazini, M., Garcia, L., Cinagawa, E., Wiechmann, S., & Carrilho, A. (2008). Prevalência da Lipodistrofia Associada ao HIV em Pacientes Ambulatoriais Brasileiros: Relação com Síndrome Metabólica e Fatores de Risco Cardiovascular. *Arquivos Brasileiros de Endocrinologia e Metabologia*, Vol. 52, No. 4, (Jun 2008), pp. (658-667), ISSN 0004-2730.

Dubé, M., Stein, J., Aberg, J., Fichtenbaum, C., Gerber, J., Tashima, K., Henry, W., Currier, J., Sprecher, D., & Glesby, M. (2003). Guidelines for the evaluation and management of dyslipidemia in human immunodeficiency virus (HIV)-infected adults receiving antiretroviral therapy: Recommendations of the HIV Medicine Association of the Infectious Disease Society of America and the Adult AIDS Clinical Trials Group. *Clinical Infectious Diseases*, Vol. 37, No. 5, (Sep 2003), pp. (613-627), ISSN 378131.

Dutra, C. & Libonati, R. (2008). Perfil metabólico e nutricional de pacientes HIV positivos com lipodistrofia submetidos à terapia anti-retroviral: Orientação Nutricional. Dissertação de mestrado. Universidade Federal do Pará. Belém-Brazil. (Abr 2008), 151pp.

Eichenbaum-Voline S., Olivier, M., Jones, E., Naoumova, R., Jones, B., Gau, B., Patel, H., Seed, M., Betteridge, D., Galton, D., Rubin, E., Scott, J., Shoulders, C., & Pennacchio, L. (2004). Linkage and association between distinct variants of the APOAI/C3/A4/A5 gene cluster and familial combined hyperlipidemia. *Arteriosclerosis, Thrombosis and Vascular Biology*, Vol. 24, No. 1, (Jan 2004), pp. (167-174), ISSN 10795642.

Friis-M øller, N., Reiss, P., Sabin, C. A., Weber, R., Monforte, A., El-Sadr, W.,Thiebaut, R.,

De Wit, S., Kirk, O., Fontas, E., Law, M. G., Phillips, A., & Lundgren, J. D. (Mai 2003). Cardiovascular disease risk factors in HIV patients - association with antiretroviral therapy. In: *Official Journal of International AIDS Society*, Acesso em 06 Jun 2011, Disponível em: <http://discovery.ucl.ac.uk/6830/1/6830.pdf>

Friis-Møller, N; Weber, R., Reiss, P; Thiébaut, R., Kirk, O., Monforte, A., Pradier, C., Morfeldt, L., Mateu, S., Law, M., El-Sadr, W., De Wit, S., Sabin, C., Phillips, A., Lundgren, J. (2003). Cardiovascular disease risk factors in HIV patients - association with antiretroviral therapy. Results from the DAD study. *AIDS*, Vol 17, No 8,(May 2003), pp. (1179-1193), ISSN: 0269-937.

Furtado, J., Zambrini, H., Neto, D., Scozzafave, G., & Brasileiro, R. (2007). Ambulatório de Lipodistrofia do Hospital Heliópolis - Uma experiência com as correções cirúrgicas em dois anos de atendimento. *Prática hospitalar*, Vol. 58, No. 28, (Set-Out IX), pp. (28-32), ISSN 1679-5512.

Galli, M., Cozzi-Lepri, A., Ridolfo, A., Gervasoni, C., Ravasio, L., Corsico, L., Gianelli, E., Vaccarezza, M., Vullo, V., Cargnel, A., Minoli, L., Coronado, O., Giacometti, A., Antinori, A., Antonucci, G., D'Arminio Monforte, A., & Moroni, M. (2002). Incidence of adipose tissue alterations in first-line antiretroviral therapy: the LipolCoNa Study. *Archives of Internal Medicine*, Vol. 22, No. 162, (Dez 2002), pp. (2621-2628), ISSN 00039926.

Garg, A. (2000). Lipodystrophies. *The American Journal of Medicine*, Vol. 108, No. 2, (Feb 2000), pp. (143-152), ISSN: 0002-9343.

Gidding, S. S. Preventive pediatric cardiology(1999). *The Pediatric Clinics North America***.** Vol. 46, No 2 (abr. 1999), pp. (253-262), ISSN:0031-3955.

Gkrania-Klotsas, E., & Klotsas, A. (2007). HIV and HIV treatment: effects on fats, glucose and lipids. *British Medical Bulletin*, Vol. 84, No. 1, (Nov 2007), pp. (49-68), ISSN 0007-1420.

Goujard, C., Vincent, I., Meynard, J., Choudet, N., Bollens, D., Rousseau, C., Demarles, D., Gillotin, C., Bidault, R., & Taburet, A. (2003). Steady-state pharmacokinetics of amprenavir coadministered with ritonavir in human immunodeficiency virus type 1-infected patients. *Antimicrobial agents and chemotherapy*, Vol. 47, No. 1, (Jan 2003), pp. (118-123), ISSN 0066-4804.

Grinspoon, S., & Carr, A. (2005) Cardiovascular Risk and Body-Fat Abnormalities in HIV-Infected Adults. *New England Journal of Medicine*, Vol. 352, No. 1, (Jan 2005), pp. (48-62), ISSN 0028-4793.

Grunfeld, C., Pang, M., Doerrler, W., Shigenaga, J., Jensen, P., & Feingold, K. (1992). Lipids, lipoproteins, triglyceride clearance, and cytokines in human immunodeficiency virus infection and the acquired immunodeficiency syndrome. *Journal of Clinical Endocrinology & Metabolism,* Vol. 74, No. 5, (May 1992), pp. (1045-1052), ISSN 0021-972X.

Hadigan, C., Kamin, D., Liebau, J., Mazza, S., Barrow, S., Torriani, M., Rubin, R., Weise, S., Fischman, A., & Grinspoon, S. (2006). Depot-specific regulation of glucose uptake and insulin sensitivy in HIV-lipodystrophy. *American Journal of Physiology, Endocrinology & Metabolism*, Vol. 2, No. 290, (Feb 2006), pp. 289-298, ISSN 0193-1849.

Haugaard, S., Andersen, O., Dela, F., Holst, J., Storgaard, H., Fenger, M., Iversen, J., & Madsbad, S. (2005). Defective glucose and lipid metabolism in human immunodeficiency virus-infected patients with lipodystrophy involve liver, muscle tissue and pancreatic beta-cells. *European Journal of Endocrinology*, Vol. 152, No. 1, (Jan 2005), pp. (103-112), ISSN 0804-4643.

Heath, K., Chan, K., Singer, J., O'shaughnessy, M., Montaner, J., & Hoogg, R. (2002). Incidence of morphological and lipid abnormalities: gender and treatment differentials after initiation of first antiretroviral therapy. *International Journal of Epidemiology*, Vol. 31, No. 5, (Oct 2002), pp.1016-1020, ISSN *0300-5771*.

Henry K, Melroe H, Huebesch J, Hermundson J, Simpson J. Atorvastatin and gemfibrozil for protease-inhibitor–related lipid abnormalities (1998). *Lancet.* Vol. 352, No 9133(Sep. 1998), pp. (1031–1032), ISSN 0140-6736.

Jones SP, Doran DA, Leatt PB, Maher B, Pirmohamed M (2001). Short-term exercise training improves body composition and hyperlipidaemia in HIV-positive individuals with lipodystrophy . *AIDS* . Vol. 15, No 15, pp. (2049–2051), , ISSN: 0269-937.

Kotler D. (2008). HIV and Antiretroviral Therapy: Lipid Abnormalities and Associated Cardiovascular Risk in HIV-Infected Patients. *Journal of Acquires Immune Deficiency Syndromes*, Vol. 53, No. 3, (Sep 2008), pp. (79-85), ISSN *1525-4135*.

Kramer, A., Lazzarotto, A., Sprinz, E., & Manfroi, W. (2009). Alterações metabólicas, terapia antirretroviral e doença cardiovascular em idosos portadores de HIV. *Arquivos Brasileiros de Cardiologia*, Vol. 93, No. 5, (Nov 2009), pp. (561-568), ISSN 0066-782X.

Liang, J., Distler, O., Cooper, D., Jamil, H., Deckelbaum, R., Ginsberg, H., & Sturley, S. (2001). HIV protease inhibitors protect apolipoprotein B from degradation by the proteasome: a potential mechanism for protease inhibitor-induced hyperlipidemia. *Nature Medicine,* Vol.7, No. 12, (Dec 2001), pp. (1327-1331), ISSN 1078-8956.

Licht, C., Vreeburg, S., van Reedt Dortland, A., Giltay, E., Hoogendijk, W., DeRijk, R., Vogelzangs, N., Zitman, F., de Geus, E., & Penninx, B. (2010) Increased sympathetic and decreased parasympathetic activity rather than changes in hypothalamic-pituitary-adrenal axis activity is associated with metabolic abnormalities *Journal of Clinical Endocrinology & Metabolism*, Vol. 95, No. 5, (May 2010), pp. (2458-2466), ISSN 0021-972X.

Lichtenstein, K. (2005) Redefining Lipodistrophy Syndrome: Risks and Impact on Clinical Decision Making. *Journal of Acquired Immune Deficiency Syndromes*, Vol. 39, No. 4, (Aug 2005), pp. (395-400), ISSN *1525-4135*.

Lihn, A., Richelsen, B., Pedersen, S., Haugaard, S., Rathje, G., Madsbad, S., & Andersen, O. (2003) Increased expression of TNF-α, IL-6, and IL-8 in HALS: implications for reduced adiponectin expression and plasma levels. *American Journal of Physiology Endocrinology & Metabology*, Vol. 285, No. 5, (Nov 2003), pp. (1072-1080), ISSN 0193-1849.

Maagaard, A., & Kvale, D. (2009). Mitochondrial toxicity in HIV-infected patients both off and on antiretroviral treatment: a continuum or distinct underlying mechanisms? *Journal of Antimicrobial Chemistry*, Vol. 64, No. 5, (Sep 2009), pp. (901-909), ISSN 0929-8673.

Mallewa, J., Wilkins, E., Vilar, J., Mallewa, M., Doran, D., Back, D., & Pirmohamed, M. (2008) HIV-associated lipodystrophy: a review of underlying mechanisms and therapeutic options. *The Journal of Antimicrobial Chemotherapy*, Vol. 62, No. 4, (Oct 2008), pp. (648-660), ISSN *0305-7453*.

Mallon, P., Miller, J., Cooper, D., & Carr, A. (2003). Prospective evaluation of the effects of antiretroviral therapy on body composition in HIV-1-infected men starting therapy. *AIDS*, Vol. 17, No. 7, (May 2003), pp. (971–979), ISSN 0269-9370.

Manninen, V., Elo, M., Frick, M., Haapa, K., Heinonen, O., Heinsalmi, P., Helo, P., Huttunen, J., Kaitaniemi, P., & Koskinen, P. (1988). Lipid alterations and decline in the incidence of coronary heart disease in the Helsinki Heart Study, *The Journal of the American Medical Association*, Vol. 260, No. 1, (1988), pp. (641-651), ISSN 00987484.

Marshall, H., Morrison, L., Wu, L., Anderson, J., Corneli, P., Stauffer, D., Allen, A., Karagounis, L., & Ward, R. (1994). Apolipoprotein polymorphism fail to define risk of coronary artery disease. Results of a prospective, angiographically controlled study. *Circulation*, Vol. 89, No. 2, (Feb 1994), pp. (567-577), ISSN 0009-7322.

Mello, A., Reis, E., & Ribeiro, R. (2008). Lipodistrofia no uso da Terapia Antiretroviral com Inibidores da Protease no HIV. *Saúde & Ambiente em Revista*, Vol. 3, No. 1, (Jan-jun 2008), pp. (66-75), ISSN 1980-2676.

Miller J, Brown D, Amin J, et al (2002). A randomized, double-blind study of gemfibrozil for the treatment of protease inhibitor–associated hypertriglyceridaemia. *AIDS.* Vol 16, No 16 (Nov. 2002), pp. (2195–2200), ISSN: 0269-937.

Ministério da Saúde do Brasil. (2008). Recomendações para terapia anti-retroviral em adultos infectados pelo HIV: manual de bolso. In: *Série A. Normas e Manuais Técnicos*, Data de acesso: Jun 2011, Disponível em: http://www.crt.saude.sp.gov.br/resources/crt_aids/arquivos_transmissao_vertical/transmissao_vertical_hiv/portarias_manuais_recomendacoes_outros/consenso_adulto_2008.pdf>.

Moyle GJ, Lloyd M, Reynolds B, Baldwin C, Mandalia S, Gazzard BG (2001). Dietary advice with or without pravastatin for the management of hypercholesterolemia associated with protease inhibitor therapy. *AIDS*. Vol. 15, No 12 (Aug 2001), pp. (503–508), , ISSN: 0269-937.

Mooser, V. & Carr, A. (2001). Antiretroviral therapy-associated hyperlipidaemia in HIV disease. *Current Opinion in Lipidology*., Vol. 12, No. 3, (Jun 2001), pp. 313-319, ISSN 0957-9672.

Mulligan, K. (2003). Metabolic Abnormalities in Patient with HIV Infection. *Journal of the International Association of Physicians in Aids Care (Chicago)*, Vol. 2, No. 2, (Apr-Jun 2003), pp. (66-74), ISSN 1545-1097.

Noor, M. (2007). The role of protease inhibitors in the pathogenesis of HIV-associated insulin resistance: cellular mechanisms and clinical implications. *Current HIV/AIDS Reports,* Vol.4, No. 3, (Dec 2007), pp. 126-134, ISSN 1548-3568.

Palacios R, Santos J, Gonzalez M, et AL (2002). Efficacy and safety of atorvastatin in the treatment of hypercholesterolemia associated with antiretroviral therapy. *Journal of Acquired Immune Deficiency Syndromes.* Vol. 30, No 5 (Aug. 2002), pp. (536–537), ISSN 1525-4135.

Parenti, C., Pereira, L., Brandão, Z., & Silvério, A. (2005). Perfil dos pacientes com AIDS acompanhados pelo Serviço de Assistência Domiciliar Terapêutica do Município de Contagem, Estado de Minas Gerais, Brasil, 2000-2003. *Epidemiologia e Serviços de Saúde*, Vol. 14, No. 2, (Jun 2005), pp. (91-96), ISSN 1679- 4974.

Pedersen, T., Olsson, A., Faergeman, O., Kjekshus, J., Wedel, H., Berg, K., Wilhelmsen, L., Haghfelt, T., Thorgeirsson, G., Pyörälä, K., Miettinen, T., Christophersen, B., Tobert, J., Musliner, T., & Cook, T. (1998). Lipoprotein changes and reduction in the incidence of coronary heart disease events in the Scandinavian Simvastatin Survival Study (4S). *Circulation,* Vol. 97, No. (1), (1998), pp. (1453-1461), ISSN 0009-7322.

Quintaes, D., & Garcia, R. (1999). Adesão de pacientes HIV positivos à dietoterapia ambulatorial**.** *Revista de Nutrição***,** Vol. 12, No. 2, (Mai-Ago 1999), pp. **(**175-181).

Rasmusson, A., Schnurr, P., Zukowska, Z., Scioli, E., & Forman, D. (2010). Adaptation to extreme stress: post-traumatic stress disorder, neuropeptide Y and metabolic syndrome. *Experimental Biology and Medicina (Maywood)*, Vol. 235, No. 10, (Oct 2010), pp. (1150-1162), ISSN 1535-3702.

Riddle, M., Kuhel, D., Woollett, L., Fichtenbaum, C., & Hui, D. (2001). HIV protease inhibitor induces fatty acid and sterol biosynthesis in liver and adipose tissues due to the accumulation of activated sterol regulatory element-binding proteins in the nucleus. *Journal of Biological Chemistry,* Vol. 276, No. 40, (Oct 2001), pp. 37514-37519, ISSN 0021-9258.

Samaras, K., Wand, H., Law, M., Emery, S., Cooper, D., & Carr, A. (2009). Dietary intake in HIV-infected men with lipodystrophy: relationships with body composition, visceral fat, lipid, glucose and adipokine metabolism. *Current HIV Research*, Vol. 7, No. 4, (Jul 2009), pp. (454-461), ISSN 1570-162X.

Santos, C., Felipe, Y., Braga, P., Ramos, D., Lima, R., & Segurado, A. (2005). Self-perception of body changes in persons living with HIV/AIDS: prevalence and associated factors. AIDS, Vol. 4, No. 1, (Oct 2005), pp. (14-21), , ISSN: 0269-937, ISSN: 0269-937.

Sattler, F. (2008). Pathogenesis and Treatment of Lipodystrophy: What Clinicians Need To Know. *Topics in HIV Medicine*, Vol. 16, No. 4, (Oct-Nov 2008), pp. (127-133), ISSN 1542-8826.

Segarra-Newnham, M. (2002). Hyperlipidemia in HIV-positive patients receiving antiretrovirals. *The Annals of Pharmacotherapy*, Vol. 36, No. 4, (Apr 2002), pp. (592-595), ISSN 1060-0280.

Seidl, E., & Machado, A. (2008). Bem-estar psicológico, enfrentamento e lipodistrofia em pessoas vivendo com HIV/aids. *Psicologia em estudo*, Vol. 13, No. 2, (Apr-Jun 2008), pp. (239-247), ISSN 1413-7372.

Shahmanesh, M., Jaleel, H., DeSilva, Y., Ross, J., Caslake, M. & Cramb, R. (Jun 2001) Protease inhibitor related type III hyperlipoproteinaemia is common and not associated with apolipoprotein-E E2/E2 phenotype. In: *Sexually Transmitted Infections,* Acesso em 04 Jun 2011, Disponível em: < http://sti.bmj.com/content/77/4/283.abstract>

Smith P, DiCenzo R, Morse G (2001). Clinical pharmacokinetics of nonnucleosidereverse transcriptase inhibitors. *Clinical Pharmacokinetics*, Vol. 40, No 12, (2001), pp. (893–905), ISSN 0312-5963.

Sposito, A., Caramelli, B., Fonseca, F., & Bertolami, M. (2007). IV Diretriz Brasileira sobre Dislipidemias e Prevenção da Aterosclerose: Departamento de Aterosclerose da Sociedade Brasileira de Cardiologia. *Arquivos Brasileiros de Cardiologia*, Vol. 88, No. 1, (Abr 2007), pp. (2-19), ISSN 1678-4170.

Sprinz, E., Lazzaretti, R., Kuhmmer, R., & Ribeiro, J. (2010). Dyslipidemia in HIV-infected individuals. *Brazilian Journal of Infectious Diseases,* Vol. 14, No. 6, (Nov 2010), pp. (575-588), ISSN 1413-8670.

Stankov, M., & Behrens, G. (2010) Contribution of Inflammation to Fat Redistribution and Metabolic Disturbances in HIV-1 Infected Patients. *Current Pharmaceutical Design*, Vol. 16, No. 30, (Out 2010), pp. (3361-3371), ISSN 1381-6128.

Tall, A. (1990) Plasma high density lipoproteins. Metabolism and relationship to atherogenesis. *The Journal of Clinical Investigation*, Vol. 86, No. 2, (Aug 1990), pp. (379-384), ISSN 00219738.

Ter Hofstede, H., Burger, D., & Koopmans, P. (2003). Antiretroviral therapy in HIV patients: aspects of metabolic complications and mitochondrial toxicity. *The Netherlands Journal of Medicine*, Vol. 61, No. 12, (Dec 2003), pp. (393-403), ISSN 0300-2977.

The HIV/Aids Treatment Information Service (ATIS). (Sep 2002). *Glossary of HIV/AIDS-Related Terms*, The HIV/Aids Treatment Information Service (ATIS), Retirado de <http://www.hiv.gov.gy/edocs/glossary.pdf>.

Thiébaut, R., Daucourt, V., Mercié, P., Ekouévi, D. K., Malvy, D., Morlat, P., Dupon, M., Neau, D., Farbos, S., Marimoutou, C., & Dabis, F. (2000). Lipodystrophy, metabolic disorders, and human immunodeficiency virus infection: Aquitaine cohort, France, 1999. Groupe d'Epidémiologie Clinique du Syndrome d'Immunodéficience Acquise en Aquitaine. *Clinical Infectious Diseases*. Vol. 31, No. 6 (Dec 2000), pp. (1482-7), ISSN 1058-4838.

Tien, P., Cole, S., Williams, C., Li, R., Justman, J., Cohen, M., Young, M., Rubin, N., Augenbraun, M., & Grunfeld, C. (2003). Incidence of lipoatrophy and lipohypertrophy in the women's interagency HIV study. *Journal of Acquired Immune Deficiency Syndromes*, Vol. 34, No. 5, (Dec 2003), pp. (461-466), ISSN 1077-9450.

Tovar, J., & Schering, D. (2006) Management of Dyslipidemia in Special Populations. *Journal of Pharmacy Practice*, Vol. 19, No. 2, (Apr 2006), pp. (63-78), ISSN 0897-1900.

Valente, A., & Valente, O. (2007). Síndrome Lipodistrófica do HIV: Um Novo Desafio para o Endocrinologista**.** *Arquivos Brasileiros de Endocrinologia e Metabologia*, Vol. 51, No. 1, (Fev 2007), pp. (3-4), ISSN 0004-2730.

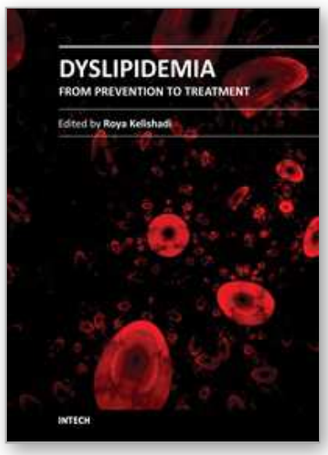
Van Griensven, J., De Naeyer, L., Mushi, T., Ubarijoro, S., Gashumba, D., Gazielle, C., & Zachariah, R. (2007). High prevalence of lipoatrophy among patients on stavudine-containing first-line antiretroviral therapy regimens in Rwanda. *Transactions of the Royal Society of Tropical Medicine and Hygiene*, Vol. 101, No. 8, (Ago 2007), pp. (793-798), ISSN 0035-9203**.**

World Health Organization (CH), United Nations Programme on HIV/Aids - UNAIDS (CH). (2009). Aids epidemic update: November 2009, In: *WHO Library Cataloguing-in-Publication Data,* Date of access: Jun 2011, Available from: <http://data.unaids.org/pub/Report/2009/jc1700_epi_update_2009_en.pdf>.

World Health Organization. (1995). Physical Status: The Use and Interpretation of Antropometry. In: *WHO Technical Report Series 854*, Date of Access: May 2011, Available from: <http://whqlibdoc.who.int/trs/WHO_TRS_854.pdf>.

Yarasheski KE, Tebas P, Stanerson B, et al (2001). Resistance exercise training reduces hypertriglyceridemia in HIV-infected men treated with antiviral therapy. *Journal of Applied Physiology*; Vol. 90, No. 1 (april 2001**)**,. pp. (133–138), ISSN 8750-7587.

Yu, P., Calderaro, D., Lima, E. & Caramelli, B. (2005). Terapia hipolipemiante em situações especiais – Síndrome de Imunodeficiência Adquirida. *Arquivos Brasileiros de Cardiologia*, Vol. 85, No. 5, (Oct 2005), pp. (58-61).



Dyslipidemia - From Prevention to Treatment

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Dyslipidemia has a complex pathophysiology consisting of various genetic, lifestyle, and environmental factors. It has many adverse health impacts, notably in the development of chronic non-communicable diseases. Significant ethnic differences exist due to the prevalence and types of lipid disorders. While elevated serum total- and LDL-cholesterol are the main concern in Western populations, in other countries hypertriglyceridemia and low HDL-cholesterol are more prevalent. The latter types of lipid disorders are considered as components of the metabolic syndrome. The escalating trend of obesity, as well as changes in lifestyle and environmental factors will make dyslipidemia a global medical and public health threat, not only for adults but for the pediatric age group as well. Several experimental and clinical studies are still being conducted regarding the underlying mechanisms and treatment of dyslipidemia. The current book is providing a general overview of dyslipidemia from diverse aspects of pathophysiology, ethnic differences, prevention, health hazards, and treatment.

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