

DISCORDANCE BETWEEN BODY MASS INDEX AND ANTHROPOMETRIC MEASUREMENTS AMONG HIV-1-INFECTED PATIENTS ON ANTIRETROVIRAL THERAPY AND WITH LIPOATROPHY/LIPOHYPERTROPHY SYNDROME

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SUMMARY

Introduction: Highly Active Antiretroviral Therapy (HAART) has improved and extended the lives of thousands of people living with HIV/AIDS around the world. However, this treatment can lead to the development of adverse reactions such as lipoatrophy/lipohypertrophy syndrome (LLS) and its associated risks. **Objective:** This study was designed to assess the prevalence of self-reported lipodystrophy and nutritional status by anthropometric measurements in patients with HIV/AIDS. **Methods:** An observational study of 227 adult patients in the Secondary Immunodeficiencies Outpatient Department of Dermatology, Hospital das Clínicas, Faculty of Medicine, University of São Paulo (3002 ADEE-HCFMUSP). The sample was divided into three groups; Group 1 = 92 patients on HAART and with self-reported lipodystrophy, Group 2 = 70 patients on HAART without self-reported lipodystrophy and Group 3 = 65 patients not taking HAART. The nutritional status of individuals in the study sample was determined by body mass index (BMI) and percentage of body fat (% BF). The cardiovascular risk and diseases associated with abdominal obesity were determined by waist/hip ratio (WHR) and waist circumference (WC). **Results:** The prevalence of self-reported lipoatrophy/lipohypertrophy syndrome was 33% among women and 59% among men. Anthropometry showed depletion of fat mass in the evaluation of the triceps (TSF) in the treatment groups with HAART and was statistically independent of gender; for men $p = 0.001$, and for women $p = 0.007$. Similar results were found in the measurement of skin folds of the upper and lower body ($p = 0.001$ and $p = 0.003$ respectively). In assessing the nutritional status of groups by BMI and % BF, excess weight and body fat were more prevalent among women compared to men ($p = 0.726$). The WHR and WC revealed risks for cardiovascular and other diseases associated with abdominal obesity for women on HAART and with self-reported LLS ($p = 0.005$ and $p = 0.011$). **Conclusions:** Anthropometric measurements were useful in the confirmation of the prevalence of LLS. BMI alone does not appear to be a good parameter for assessing the nutritional status of HIV-infected patients on HAART and with LLS. Other anthropometric measurements are needed to evaluate patients with the lipoatrophy/lipohypertrophy syndrome.

KEYWORDS: HIV; Lipoatrophy/lipohypertrophy syndrome; Nutrition; Anthropometry; Brazil.

INTRODUCTION

The widespread use of Highly Active Antiretroviral Therapy (HAART) has promoted a sustained reduction in both morbidity and mortality associated with HIV-1^{20,33}. Although the curve of the HIV epidemic has been showing signs of flattening around the world, HIV infection remains almost invariably fatal if the individuals are not treated with HAART^{6,33,38}.

Despite the increases in the availability of HAART, other challenges related to the management of patients with HIV are just beginning to surface. For example, HAART itself can cause a variety of adverse effects such as the lipoatrophy/lipohypertrophy syndrome^{3,4,8,9}. Such an

occurrence may contribute to a decrease in adherence to antiretroviral therapy, adding to the difficulties inherent to prolonged treatment with combinations of drugs which characterize HAART¹⁴. Moreover, both the changes in the composition and distribution of body fat may negatively affect self-image, thus interfering with treatment adherence and contributing to possible therapeutic failure^{2,9}.

Although there is no consensus on the prevention or treatment of the lipoatrophy/lipohypertrophy syndrome, the World Health Organization has indicated that nutrition should be a part of all programs for control and treatment of HIV/AIDS, since diet and adequate nutritional status can improve adherence and effectiveness of treating patients on HAART^{10,36}. The identification of early morphological changes for these patients

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through the assessment and diagnosis of their nutritional status can help to establish effective interventions for the treatment of metabolic and morphological reactions^{14,31}. Identification and appropriate treatment for these conditions can both improve patients' long-term care and help provide a better outlook for their quality of life^{2,19,21}.

According to the American Dietetic Association, anthropometry has been widely used to assess the health and nutritional status of individuals, communities or populations, not only due to its simplicity and low cost, but also because it can provide an approximation of body composition and distribution of body fat^{1,15,18}. The aim of this study was to assess the prevalence of self-reported lipoatrophy/lipohypertrophy and nutritional status by anthropometric measurements in patients with HIV/AIDS in a cohort of outpatient HIV-infected persons in São Paulo, Brazil.

MATERIAL AND METHODS

This observational study was based on data collected between September 2006 and July 2008 from a referral center for the treatment of HIV infection in São Paulo, Brazil, in the Secondary Immunodeficiencies Outpatient Department of Dermatology, Hospital das Clínicas, Faculty of Medicine, University of São Paulo (ADEE 3002-HCFMUSP). The study was approved by the Research Ethics Committee of the University of São Paulo Medical School (Research Protocol No. 0221/07).

This open cohort consists of 320 HIV-1-positive patients who have been followed since 1989. The sample consisted of 227 subjects (71% of the cohort) divided into three groups:

Group 1 = 92 HIV-1-positive patients on HAART and with self-reported lipoatrophy/lipohypertrophy syndrome (LLS); Group 2 = 70 HIV-1-positive patients on HAART without self-reported LLS; Group 3 = 65 HIV-1-positive patients without HAART.

The characterization of groups in terms of self-reported lipodystrophy was conducted through a questionnaire to identify socio-demographic, clinical characteristics, as well as a specific question for the patient to determine if he/she had observed bodily changes consistent with LLS after the initiation of HAART. Study inclusion criteria were HIV infection, willingness to sign the consent form and no constraint for the test performance of bioimpedance (BIA). Exclusion criteria were pregnancy, known cardiovascular disease or previous heart surgery and refusal to sign the consent form. All the patients were interviewed by the first Author using an adapted questionnaire to identify morphological body modifications after the initiation of HAART.

Anthropometric methods, which included body mass index (BMI), waist/hip ratio (WHR), waist circumference (WC) as well as an estimate of body fat percentage (BF%), were used to evaluate the nutritional status of patients and possible changes in the deposition of fat in specific areas of the body. In addition, bioelectrical impedance (BIA) was also performed^{8,11,13}.

BMI was calculated as the ratio of the current weight (kg) by height (m) squared^{16,17,39}. BF% was calculated as the sum of skinfolds of upper and lower limbs. The nutritional status was classified according to WHO recommendations for adults³⁷.

The assumed value of triceps skinfold (TSF), (mm²), was the average of three measurements and percentages¹⁶, by sex and age. The nutritional status classification was determined according to the recommendations of BLACKBURN and THORNTON⁵. Skinfold measurements were performed on the triceps, biceps, subscapular, abdominal, iliac, thigh and calf. These were obtained with the aid of the caliper Cescorf® (Cescorf, Porto Alegre, Brazil) and rounded to the nearest 0.5 mm and made in duplicate for each type of measurement¹⁶. Classification of % BF was based on recommendations made by GALLAGHER *et al.* by means of prediction equations¹⁷.

The percentage of body fat (% BF) was determined both as above described and by electrical impedance analysis (BIA) (Systems Inc. 101Q, RJL Systems, Clinton Township, MI). For examination of the BIA, the measurements were made on the right side of the body and patients were asked about restrictions for the performance of these tests¹². Measurements were performed according to the instructions in the user manual from CompCorp. The values of resistance and inductance were interpreted by software from Vcorp¹¹. Using the IDF classification, WC cutoffs were used for the diagnosis of metabolic syndrome^{25,26}. All measurements were done by one of the Authors (LS).

In addition to anthropometric data, socio-demographic characteristics were recorded as categorical and continuous variables: gender, age, education, social interaction, marital status, housing conditions, income and employment status, total duration of HAART, CD4 T-cell count, length of time from the first positive HIV test, the current HIV viral load and the presence of self-reported lipoatrophy/lipohypertrophy.

Statistical analyses were performed using the software Minitab® 15m to verify that changes in nutritional status and body fat distribution were related to gender, use of HAART and presence of lipoatrophy/lipohypertrophy³⁰. These were performed by descriptive analysis. To evaluate the association between categorical variables, the chi-square test was used. For the relationship between quantitative and categorical variables with normal distribution, the Student t-test (for two variables) was used. An association was made between variables of the study (anthropometrics and body fat distribution) according to defined groups (G1, G2, G3) and analyzed by ANOVA (used for three variables), with a confidence level of 95% and 5% significance according to the Tukey test for comparison.

RESULTS

The average age of the 227 study subjects was 42.5 years with 75 (33%) being female. Average length of education was 11 years and most subjects shared a residence with three or more persons. The majority of men were single individuals. Over half of the patients own their own homes with proper sanitation and the per capita income was one to five times the minimum wage. There was no statistically significant difference by gender for these variables. Self-reported prevalence of the LLS was 33% among women and 59% among men (Table 1).

In Table 2, it is noted that this group had, on average, longer use of HAART, a higher T CD4 cell nadir, and more years of clinical follow-up compared with those without self-reported lipodystrophy and those not taking HAART. Analysis of triceps skinfold (TSF) found a depletion

Table 1
Socio-demographic characteristics of the 227 HIV-1-infected individuals by gender

Variable	Males (152)	Females (75)	p value
Age (Mean ± SD), years	43 ± 8	42 ± 9	NS
Years of schooling			NS
Unknown	13 (8.55)	5 (6.66)	
None	1 (0.65)	1 (1.33)	
≤ 8 years	41 (26.97)	22 (29.33)	
9-11 years	62 (40.78)	39 (52)	
>11 years	38 (25)	7 (9.33)	
Home sharing			NS
Unknown	12 (7.89)	5 (6.66)	
No	34 (22.36)	4 (5.33)	
With 2 persons	31 (20.39)	13 (17.33)	
With more than 2 persons	74 (48.68)	52 (69.33)	
Marital status			NS
No answer	15 (9.86)	6 (8)	
Single	83 (54.60)	20 (26.66)	
Married	24 (15.78)	20 (26.66)	
Divorced	9 (5.92)	17 (22.66)	
Home ownership			NS
No answer	15 (9.86)	8 (10.66)	
Owner	82 (53.94)	42 (56)	
Tenant	44 (28.94)	20 (26.66)	
Other	11 (7.23)	4 (5.33)	
Employment condition			NS
No answer	10 (6.57)	6 (8)	
Employed	103 (67.76)	42 (56)	
Unemployed	39 (25.65)	27 (36)	
Income (minimum wage)			NS
None	10 (6.57)	12 (16)	
< 1	11 (7.23)	13 (17.33)	
1-5	97 (63.81)	36 (48)	
6-10	16 (10.52)	6 (8)	
> 10	4 (2.63)	-	
No answer	13 (8.55)	7 (9.33)	
Self reported body changes	59 (38.81%)	33 (44%)	

NS: Not statistically significant when *p* value > 0.05; Income: 1 minimum wage = ~ US\$300.00.

of fat mass in groups undergoing treatment with HAART and this result was statistically significant when compared to the group without HAART (for men *p* = 0.001, for women *p* = 0.007). A similar result was determined in the analysis of skin folds of the upper and lower limbs, where groups using HAART had greater loss of fat tissue which was statistically significant compared to Group 3 (*p* = 0.001) (*p* = 0.003). In the assessment of nutritional status by BMI, the majority of men were eutrophic. However this result was not statistically significant between groups (*p* = 0.72). Similarly, measurement of the sum of skinfolds revealed excess body fat tissue in all groups. Men on HAART and with self-reported lipodystrophy were identified by WHR measurements as having statistically significant higher risk for cardiovascular diseases when compared to those without LLS (*p* = 0.0001). However, when the comparison refers to CA ≥ 90 cm no significant difference was found between men in the three groups.

For women under HAART and with lipodystrophy, the measurements for WHR and CA showed a higher risk for cardiovascular diseases (*p* = 0.005 and *p* = 0.01, respectively).

DISCUSSION

The strengthening of social support, adherence to treatment and the establishment of life goals are important factors in the quality of life for those living with HIV³⁹. The socio-demographic characteristics of this study reflect the epidemiological trends of HIV in Brazil. With a ratio of two men to one woman, an increasing number of women were observed, mainly due to heterosexual transmission of HIV being observed more recently⁶. Most patients in this study have, on average, some level of school education, and most are employed with reasonably stable incomes and good social status, unlike other groups of patients with HIV in Brazil who predominantly have a low level of education and poor social conditions.

Overall, body changes have been reported in 20-80% of patients on HAART, consisting primarily of Caucasian males, which roughly agrees with the results of this study^{7,22}. When subcutaneous fat of the upper and lower limbs was estimated by TSF, a depletion of fat mass was found in groups undergoing treatment by HAART. These results support the hypothesis that morphological changes associated with lipodystrophy of the upper and lower limbs are common among HIV-infected individuals undergoing HAART. There are no standardized criteria for the diagnosis of LLS and such changes are clinically evident approximately six to 24 months after HAART^{28,29,33}.

To identify changes in the distribution of body fat, monitoring of skinfolds has been recommended^{5,23,24}. According to HEYWARD & STOLARCKZYK, these anthropometric measurements have been used in studies focusing on HIV/AIDS in developed countries, yet currently there is little published data using the sum of skinfolds for the distribution of fat per body segment in adults with HIV infection^{10,26,33}.

A study by SANCHES³⁶ also found that 57% of their sample showed accumulation of abdominal fat, 55% had decreased peripheral fat with loss of subcutaneous tissue in the arms, legs and buttocks, and 33% stated that if they knew their physical appearance would acquire such a form, they would have opted not to begin treatment despite being aware of the risks to their health.

Table 2
Cardiovascular risk according to sex, anthropometric variables and self-reported groups of lipoatrophy/lipohypertrophy syndrome (LLS)

Variables	Males			p value	Females			p value
	Group 1	Group 2	Group 3		Group 1	Group 2	Group 3	
Subjects	59	52	41		33	18	24	
Years under HAART	7 ± 4	5 ± 4	-	0.02	7 ± 4	4 ± 5		0.01
Nadir TCD4 cells (cells/mm³)	542 (335-732)	359 (187-503)	431 (287-628)	0.01	427 (310-607)	342 (267-468)	474 (396-804)	0.04
Median (Q1-Q3)								
Time of HIV infection since diagnosis	9 ± 5	5 ± 4	2 ± 3	0.001	9 ± 5	5 ± 5	5 ± 6	0.003
HIV viral load (copies/MI)	400 (400-1053)	400 (400-3309)	15000 (1993-65675)	0.000	436 (400-6178)	400 (138-1576)	4410 (1632-14350)	0.009
TSF				0.001				0.007
Depletion	50 (84.74%)	42 (80.76%)	20 (48.78%)		26 (78.78%)	15 (83.33%)	12 (50%)	
Eutrophic	4 (6.77%)	6 (11.53%)	3 (7.31%)		6 (18.18%)	3 (16.66%)	4 (16.66%)	
Excess	5 (8.47%)	4 (7.69%)	17 (41.46%)		1 (3.03%)	-	8 (33.33%)	
% folds members	32 ± 7	35 ± 9	38 ± 7	0.001	39 ± 9	45 ± 8	46 ± 7	0.003
Mean ±SD								
BMI				0.72				0.05
Depletion	-	-	-					
Eutrophic	32 (54.23%)	28 (53.84%)	20 (48.78%)		-	1 (5.55%)	-	
Excess	27 (45.76%)	24 (46.15%)	20 (48.78%)		12 (36.36%)	13 (72.22%)	12 (50%)	
% fat by Durnin				0.03				0.014
Depletion	-	-	1 (2.43%)		-	-	-	
Eutrophic	4 (6.77%)	16 (30.76%)	6 (11.53%)		-	-	1 (4.16%)	
Excess	53 (89.83%)	33 (63.46%)	31 (75.60%)		33 (100%)	18 (100%)	23 (95.83%)	
% fat by BIA				0.13				0.19
Depletion	4 (6.77%)	-	3 (7.31%)		-	-	-	
Eutrophic	22 (37.28%)	26 (50%)	9 (21.95%)		4 (12.12%)	5 (27.77%)	2(8.33%)	
Excess	33 (55.93%)	25 (48.07%)	27 (65.85%)					
Cardiovascular risk assessed by waist/hip ratio				0.001				0.005
Low and Intermediate	27 (45.76%)	32 (61.53%)	28 (68.29%)		2 (6.06%)	4 (22.22%)	5 (20.83%)	
High and very high	32 (54.23%)	20 (38.46%)	12 (29.26%)		31 (93.93%)	14 (77.77%)	19 (79.16%)	
Cardiovascular risk assessed by waist circumference according to WHO				0.63				0.01
Low and intermediate	52 (88.13%)	49 (94.23%)	35 (85.36%)		11 (33.33%)	11 (61.11)	13 (54.16%)	
High	5 (8.47%)	3 (5.76%)	5 (12.19%)		22 (66.66%)	7 (38.88%)	5 (20.83%)	
Cardiovascular risk assessed by waist circumference - according to IDF				0.63				0.01
Men ≥ 90 and women ≥ 80	30 (50.84%)	24 (46.15%)	18 (43.90%)		30 (90.90%)	10 (55.55%)	19 (79.16%)	

SD = Standard Deviation. Group 1 = Self-reported lipoatrophy/lipohypertrophy and HAART. Group 2 = HAART and no lipoatrophy/lipohypertrophy and Group 3 = Not on HAART. For relationships between categorical and quantitative variables with normal distribution the t student's test was used (for two variables). The association between the study variables (anthropometry and body fat distribution) was performed according to defined groups (G1, G2 and G3) and analyzed by ANOVA (used for 3 variables), with a confidence level of 95% and significance of 5%, according to the comparison test of Tukey.

The cardiovascular risk associated with obesity has been defined by observational evidence, especially in cohort and case-control studies such as the Nurses' Health Study, which showed a relative risk of death of 1.6 to 2.2 associated with a BMI between 27 and 32, compared to the group with BMI < 19. The NHANES Study - National Health and Nutrition Examination Survey- reported a 1.5 relative risk for CVD later in life for women with BMI > 29, compared to a reference population with BMI < 21⁴⁰.

Although BMI is employed in most population studies because of ease of use, it does not provide enough data to accurately assess body composition. Thus, there is an increased interest in measurements that best describe the amount of body fat and its relationship with obesity. BMI in itself provides only an incomplete picture of cardiovascular risk since it does not identify individuals with abdominal obesity^{18,32,34}.

This study found a high prevalence of increased body fat (BF) and

of individuals described as overweight when assessed by BMI and by their percentage of BF, particularly women undergoing HAART and with self-reported lipodystrophy. Additionally for this group, high values of WHR and of Abdominal Circumference point to a high cardiovascular risk.

Among 223 HIV-infected individuals aged 20-59 from the city of São Paulo, the prevalence of central obesity was 45.7%, with women having a higher prevalence of abdominal obesity and overweight status when compared to men, coinciding with the results of this study^{7,27}. The author also cites previous studies with patients treated using protease inhibitors showing that the accumulation of fat is often higher among women^{12,15}. Also, the development of male body patterns has been reported in most women with LLS^{15,20}. Such results agree with the findings of the present research.

Despite the limitations of this study, such as sample size, study design and cohort effect, the results indicate that other anthropometric measurements in addition to BMI are important for assessing the nutritional status of patients with LLS undergoing HAART. Insights regarding the relative value of using multiple measurements to assess the nutritional status of HIV-infected individuals were obtained. Thus, the analysis of skinfold thickness, which should be a practice adopted by all multidisciplinary teams, can help identify individuals at high risk for lipoatrophy/lipohypertrophy syndrome and for concurrent metabolic alterations.

CONCLUSIONS

- Anthropometric assessment through skinfold measurements proved to be a good method for determining loss of fatty tissue in the upper and lower limbs, regardless of gender, in HIV-infected patients undergoing HAART.
- The BMI alone does not seem to be an adequate parameter for assessing the nutritional status of HIV-infected patients undergoing HAART and the lipoatrophy/lipohypertrophy syndrome. Other anthropometric measurements are needed to evaluate patients with the syndrome.
- There was a strong association between self-reported lipoatrophy/lipohypertrophy syndrome, HAART, body composition, and cardiovascular disease risk associated with abdominal obesity.
- These studies have identified the need to perform a variety of measurements to assess the nutritional status of persons living with HIV/AIDS in clinical practice.

AUTHOR'S CONTRIBUTIONS

All authors read and contributed to this manuscript. All authors have made substantial contributions to all of the following: (1) the conception and design of the study, or acquisition of data, or analysis and interpretation of data: LRS, JC; DCS, LAMF, AJDS; FGP. (2) drafting the article or revising critically important intellectual content: LRS, JC. (3) final approval of the version to be submitted: LRS, JC; DCS, AJDS; CRG; FGP, LAMF. The authors declare not to have any conflict of interest.

RESUMO

Discordância entre o índice de massa corporal e outras medidas antropométricas em pacientes infectados pelo HIV com a síndrome de lipoatrofia/lipohipertrofia em uso de medicação antirretroviral

Objetivos: A terapia antirretroviral altamente ativa (HAART) tem melhorado e aumentado a vida de milhares de pessoas que vivem com a infecção pelo HIV/AIDS em todo o mundo. No entanto, este tratamento pode levar ao desenvolvimento da síndrome da lipodistrofia (LDS). Este estudo foi desenvolvido para avaliar a prevalência de auto-relato de LDS, perfil nutricional e medidas antropométricas de pacientes com HIV/AIDS. **Métodos:** Estudo observacional de 227 pacientes adultos, divididos em: Grupo 1: 92 pacientes em HAART e com LDS; Grupo 2: 70 pacientes em tratamento com HAART e sem LDS e Grupo 3: 65 pacientes que não tomam HAART. O estado nutricional foi avaliado pelo índice de massa corporal (IMC) e o percentual de gordura corporal (%GC) por meio de medidas antropométricas. **Resultados:** A prevalência de auto-relato de LDS foi de 44% entre as mulheres e 39% entre os homens. DC do tríceps (PCT) apresentou-se mais elevada no grupo HAART e LDS (homens $p < 0,001$; mulheres $p < 0,007$) em comparação com aqueles sem HAART, respectivamente. IMC revelou excesso de peso para a maioria dos indivíduos. **Conclusões:** As medidas antropométricas foram úteis para confirmar a prevalência de auto-relato da síndrome da lipodistrofia. A avaliação das dobras dos braços e pernas revelou-se um bom método para avaliação antropométrica de lipoatrofia de membro, independentemente do sexo. Estes resultados permitiram o estabelecimento de estratégias para o diagnóstico precoce da LDS na prática clínica, em pessoas vivendo com HIV / AIDS.

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