

Prevalence of HIV-Associated Lipodystrophy in Brazil: A Systematic Review of the Literature

Lunara Basqueroto Della Justina¹, Daisson José Trevisol^{1,2} and Fabiana Schuelter-Trevisol^{1,2*}

¹Postgraduate Program in Health Sciences, University of Southern Santa Catarina at Tubarão, Santa Catarina, Brazil

²Clinical Research Center, Hospital Nossa Senhora da Conceição, Tubarão, Santa Catarina, Brazil

Abstract

Background: Currently, AIDS is considered a chronic, treatable disease for those who have access to Highly Active Antiretroviral Therapy (HAART). However, the decline in morbidity and mortality rates with an increase in life expectancy attributable to drug treatment has adverse effects associated with its continued use, such as changes in the body-fat distribution and metabolic abnormalities that define lipodystrophy syndrome.

Objective: To conduct a systematic review of the prevalence of and methods used for defining and grading lipodystrophy in individuals living with HIV in Brazil.

Methods: The electronic search was performed in Medline, Lilacs, SciELO, and thesis and dissertation databases. Original observational studies that had determined the prevalence of lipodystrophy in HIV-infected patients were included.

Results: 103 articles were retrieved, and 16 were included in this review. The prevalence of lipodystrophy ranged between 32.4% and 88.6%. The methods used to assess lipodystrophy were: (i) Patient self-report and physician examination; (ii) patient self-report alone; (iii) physician examination and anthropometric measurements; (iv) patient self-report and anthropometric measurements; and (v) physician examination alone.

Conclusion: The weighted average prevalence of lipodystrophy was 53.5%, and the most commonly used method to assess lipodystrophy was the patient self-report and physician examination. Further longitudinal and diagnostic studies should be conducted to determine the incidence and accuracy of lipodystrophy.

Keywords: Lipodystrophy; HIV; Acquired Immune Deficiency Syndrome; Prevalence

Introduction

The acquired immunodeficiency syndrome (AIDS) is currently considered a chronic, treatable disease, and is a major public health problem worldwide [1]. Since the advent of Highly Active Antiretroviral Therapy (HAART) in 1996, a decline in morbidity and mortality rates associated with the infection by the human immunodeficiency virus (HIV) occurred, prolonging life expectancy and improving the quality of life of these individuals [2,3]. However, HAART has adverse effects associated with its continued use, such as change in body-fat distribution and metabolic disturbances [3,4].

HIV-associated lipodystrophy syndrome is the set of morphological changes in body-fat distribution and/or metabolic disorders, including lipodystrophy, dyslipidemia, insulin resistance and hyperglycemia [5-7]. These changes are associated with increased risk of developing cardiovascular disease [8].

Lipodystrophy is characterized by body-fat redistribution in individuals living with HIV and can be classified into three categories: lipohypertrophy, lipoatrophy and combined form. Morphologic changes in lipohypertrophy include enlarged abdomen caused by visceral fat accumulation, breast enlargement, and fat accumulation in the dorsocervical area. The peripheral lipoatrophy or atrophy refers to the loss of subcutaneous adipose tissue in the face, arms, legs, and buttocks, and may present prominent blood vessels. Lipoatrophy and lipohypertrophy can occur together (mixed pattern) [6]. Nevertheless, a recent study that reviewed the pathogenesis of obesity-induced metabolic syndrome discovered that lipodystrophy and metabolic syndrome constitute a group of metabolic disorders, which cause similar clinical manifestations.

They found that the problem was the lack of an adipose tissue metabolically active. HIV-infected patients can present with lipodystrophy or obesity, but the combined form does not occur among the general population [9].

The pathogenesis of lipodystrophy in people living with HIV is multifactorial and is still not completely understood. There is a considerable potential for interaction between antiretroviral drugs and HIV infection, genetic factors and lifestyle of the individual [10-13].

Changes in physical appearance associated with lipodystrophy in individuals living with HIV have a negative psychosocial impact, such as low self-esteem, social isolation and depression affecting the individual's quality of life, and may also impair adherence to treatment [14,15].

The aim of this study was to review systematically the available epidemiological data about the prevalence of lipodystrophy in the Brazilian adult population infected with HIV.

***Corresponding author:** Fabiana Schuelter Trevisol, Avenida José Acácio Moreira, 787, Bairro Dehon, Tubarão – SC CEP 88704-900, Brazil, Tel: 48-3631-7239; E-mail: fastrevisol@gmail.com

Received June 30, 2014; **Accepted** September 03, 2014; **Published** September 13, 2014

Citation: Justina LBD, Trevisol DJ, Schuelter-Trevisol F (2014) Prevalence of HIV-Associated Lipodystrophy in Brazil: A Systematic Review of the Literature. J AIDS Clin Res 5: 347. doi:10.4172/2155-6113.1000347

Copyright: © 2014 Justina LBD, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Methods

Research questions

What is the prevalence of lipodystrophy among HIV-infected adults taking or not taking antiretroviral treatment in Brazil? What method is used to determine the presence of lipodystrophy?

Search strategy

A systematic review of original observational studies, which were the available data, on the prevalence of lipodystrophy in people living with HIV in Brazil was carried out. The following keywords were used: HIV (MeSH) or Acquired Immunodeficiency Syndrome (MeSH) and Lipodystrophy MeSH and Prevalence MeSH and Brazil textline, in English and the corresponding words in Portuguese, without limiting the publication date range. The electronic search was conducted in the Medline, Lilacs and SciELO databases, in the thesis and dissertation databases of the Coordination for the Improvement of Higher Education Personnel (CAPES). The references of the selected articles were examined for possible inclusion of additional articles. The search was conducted by two independent reviewers between December 2012 and February 2013.

Eligibility criteria

We included original scientific articles that presented data on the prevalence of lipodystrophy in adults living with HIV in Brazil, and that reported the measurement method for the determination of lipodystrophy. However, there was no restriction regarding either the publication date or the language in which it was written.

We excluded studies that addressed animal studies, reports or case series, review articles, letters to the editor, those focusing only on metabolic changes or validation studies of methods for lipodystrophy assessment, with no data available on the prevalence and study population. Although cross-sectional studies remain the ideal study design for the determination of prevalence, we have reviewed other types of observational studies to examine if prevalence data were available. Duplicate articles were excluded. We started reading the titles, then the abstracts, and later the full texts. Exclusion criteria were applied at all stages, always by consensus between two readers.

Data extraction

The selected studies were analyzed to characterize the following items: author, year of publication, place and time of data collection, type of study, study population and sampling (number of investigated subjects, mean age and gender of participants), prevalence of lipodystrophy (by subtype, if available) and the method used to assess lipodystrophy.

Quality appraisal

To calculate the mean age and the prevalence of HIV-associated lipodystrophy, we used descriptive statistics to find the weighted mean, taking into account the sample size of each study.

Because HIV-associated lipodystrophy is a relatively recent phenomenon and there are few studies on the subject, we chose to include all articles and theses in this review. However, to evaluate the quality of the studies, we reported the journal's impact factor, in addition to the Strengthening Reporting of Observational studies in Epidemiology (STROBE) for the required verification items [16]. The checklist for cross-sectional studies was used, assigning two points for each recommendation fulfilled; one point for every recommendation

partially fulfilled; and zero for cases in which the recommendation was not met, totaling 22 items, ranging from 0 to 44 points.

Results

Study selection

The electronic search retrieved 103 studies, of which 73 articles and 30 theses or dissertations. After applying the inclusion and exclusion criteria, 15 manuscripts remained, of which 3 master's theses and 12 scientific papers (Figure 1).

Study characteristics

Table 1 shows the characteristics of the Brazilian studies included in the review with estimates of prevalence of lipodystrophy in people living with HIV. With regard to the study design, 14 were cross-sectional studies [17-31], and 1 was a retrospective cohort study [19].

The main objective of most reviewed studies was to identify the prevalence of lipodystrophy in people living with HIV in Brazil [17,18,23,29-31]. The remaining papers were intended to assess metabolic changes, and lipodystrophy was a secondary outcome [19-22,24-28].

A total of 5,930 male and female adults living with HIV were surveyed. The sample size in the reviewed studies ranged from 42 [23] to 1,240 [31]. The overall median age was 40.2 years, with ages ranging from 18 [19] to 78 [24] years. Only one study did not show the median age of the participants [23]. In total, there were 3,484 (58.8%) male participants.

Table 2 presents the ratings of journals according to the impact factor and the STROBE criteria. The median STROBE score of the 12 reviewed articles was 28, ranging between 21 and 35. Table 2 also

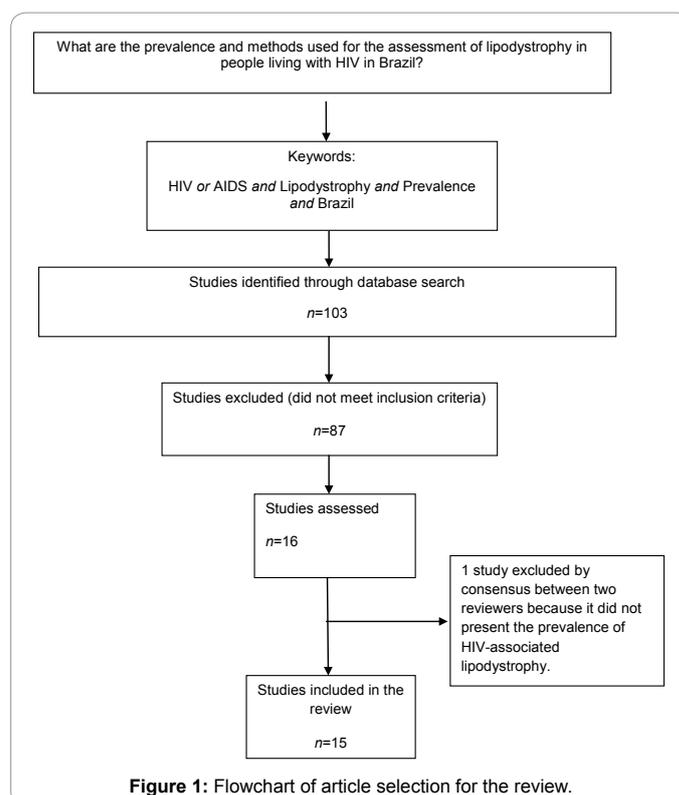


Figure 1: Flowchart of article selection for the review.

Reference	Research population, setting and study period	Study design and sample size	Gender, age (mean \pm SD)	Diagnostic methods	Prevalence of lipodystrophy
Santos CL et al. [16].	HIV/AIDS outpatients attending the Aids Hospital of the University of São Paulo Medical School, Brazil. September to December 2001.	Cross-sectional study <i>n</i> =457	71.4% men. Mean age 38 years, ranging between 19-74.	Presence of symptoms subjectively reported by patients.	64.3% Lipohypertrophy=49.2% Lipoatrophy=37.4% Mixed=22.3%
Diehl LA et al. [17].	Patients attending the outpatient clinic of infectious diseases of the Clinical Hospital, State University of Londrina, Paraná, Brazil. June 22 to November 23, 2006.	Cross-sectional study <i>n</i> =180	58.9% men. Mean age 42.9 \pm 10.5 years.	Patient self-report and physician confirmation.	55%
Monnerat BZ et al. [18].	Patients on Antiretroviral therapy recruited from the outpatient clinic at the University Hospital Cassiano Antonio de Moraes, Vitória, Espírito Santo, Brazil. July 2004 to May 2005.	Retrospective cohort study <i>n</i> =96	60.7% men. Mean age 39.2 years.	Patient self-report and physician confirmation.	59.3%
De Carvalho EH et al. [19].	Patients attending the HIV/AIDS outpatient center, University Hospital Oswaldo Cruz, Recife, Pernambuco, Brazil. July to December 2007.	Cross-sectional study <i>n</i> =256	62.1% men. Mean age 41 \pm 9.2 years.	Presence of symptoms subjectively reported by patients.	50.9%
Arruda Júnior EV et al. [20].	Patients attending the outpatient center of Oswaldo Cruz University Hospital, University of Pernambuco and the clinic center of Correia Picanço Hospital, state of Pernambuco, Brazil. June 2007 to December 2008.	Cross-sectional study <i>n</i> =958	61% men. Mean age 39.6 \pm 10 years.	Presence of symptoms subjectively reported by patients.	47% (<i>n</i> =468)
Trinca JR et al. [21].	Patients attending the Hospital de Clínicas of Porto Alegre, Rio Grande do Sul, Brazil. Unspecified study period.	Cross-sectional study <i>n</i> =410	54.6% men. Mean age 43 \pm 9.4 years.	Presence of clinical signs observed on examination by a physician.	53.4% Lipohypertrophy=26.5% Lipoatrophy=38.8% Mixed=34.7%
Segatto AFM et al. [22].	Patients on antiretroviral therapy enrolled in the Counseling and Testing Center of Presidente Prudente, São Paulo, Brazil.	Cross-sectional study <i>n</i> =42	54.8% men. Age ranged between 31 and 59 years.	Patient self-report and physician confirmation.	42.9%
Ceccato MGB et al. [23].	Medical records of patients on antiretroviral therapy treated at the Reference Center Sagrada Família, Belo Horizonte, Minas Gerais, Brazil. From 2002 to 2006.	Cross-sectional study <i>n</i> =620	66.5% men. Mean age 39.2 \pm 9.9 years, ranging from 18 to 78 years.	Presence of clinical signs observed on examination by a physician.	32.4%
Gasparotto AS et al. [24].	Referral service for the treatment of HIV in three cities of Rio Grande do Sul: Porto Alegre, Pelotas, and Rio Grande, Brazil.	Cross-sectional study <i>n</i> =614	55.5% men. Mean age 42.6 \pm 9.5 years.	Presence of clinical signs observed on examination by a physician.	51.1% (<i>n</i> =578) Lipohypertrophy=25.3% Lipoatrophy=42.1% Mixed=32.6%
Signorini DJHP et al. [25].	Patients recruited from the Immunology Laboratory of the University Hospital Graffée Guinles and the Federal University of Rio de Janeiro, Brazil. January to May 2005.	Cross-sectional study <i>n</i> =819	54.6% men. Mean age 41 \pm 11 years.	Patient self-report and physician confirmation.	38.5% (<i>n</i> =727) Lipohypertrophy=12.1% Lipoatrophy=45.0% Mixed=42.9%
Signorini DJHP et al. [26].	Patients on initial antiretroviral therapy, attending an outpatient center of a public hospital in Rio de Janeiro, Brazil. November 2006 to October 2009.	Cross-sectional study <i>n</i> =187	73% men Mean age 42 years.	Patient self-report and physician confirmation.	45.5%
Ponte CMM [27].	Patients recruited from the HIV/AIDS outpatient center for infectious diseases of São José Hospital, Fortaleza, Ceará, Brazil. January to June 2010.	Cross-sectional study <i>n</i> =144	64.6% men Mean age 42.1 \pm 7.6 years.	Patient self-report and physician confirmation.	39.4% Lipohypertrophy=14.6% Lipoatrophy=28.8% Mixed=14.4%
Soares LR [28]	Secondary Immunodeficiency Outpatient Unit, Department of Dermatology, Hospital de Clínicas, University of São Paulo School of Medicine, Brazil. June 2007 to December 2008.	Cross-sectional study <i>n</i> =227	67% men Mean age 42.7 \pm 8.3, ranging from 20 to 66 years.	Presence of symptoms subjectively reported by patients.	40.5%
Freitas E [29]	Patients recruited from a specialized care center of São Vicente, São Paulo, Brazil. July 2010.	Cross-sectional study <i>n</i> =130	43.1% men. Mean age 42.3 \pm 10.5 years.	Patient self-report and physician confirmation.	88.6% Lipohypertrophy=34.4% Lipoatrophy=7.5% Mixed=46.7%
Schuelter-Trevisol, F [30]	Patients attending a specialized care center of the State Secretary of Health, the Parthenon Sanatorium Hospital, Porto Alegre, Rio Grande do Sul, Brazil. From 2006 to 2008.	Cross-sectional study <i>n</i> =1240	50.6% men. Mean age 39.1 \pm 10.1 years.	Patient self-report and physician confirmation.	74.2% Lipohypertrophy 46% Lipoatrophy 53.2%

Table 1: Characteristics of the reviewed studies and estimates of the prevalence of HIV-associated lipodystrophy.

Reference	Journal	Impact Factor	Strobe
Santos CL et al. [16]	AIDS (London)	6.407	35
Diehl LA et al. [17]	Brazilian Archives of Endocrinology and Metabolism	0.879	24
Monnerat BZ et al. [18]	The Brazilian Journal of Infectious Diseases	1.036	25
De Carvalho EH et al. [19]	Metabolic Syndrome and Related Disorders	1.652	35
Arruda Júnior EV et al. [20]	Arquivos Brasileiros de Cardiologia	0.835	28
Trinca JR et al. [21]	Journal of Acquired Immune Deficiency Syndrome	4.653	32
Segatto AFM et al. [22]	Journal of Brazilian Society of Tropical Medicine	0.509	23
Ceccato MGB et al. [23]	Brazilian Journal of Medical and Biological Research	1.139	30
Gasparotto AS et al. [24]	AIDS (London)	6.407	30
Signorini DJHP et al. [25]	Journal of the Brazilian Medical Association	0.622	22
Signorini DJHP et al. [26]	Journal of the Brazilian Medical Association	0.622	21
Schuelter-Trevisol, F. [30]	Journal of AIDS and Clinical Research	6.83	31
Reference	University	Type of Document	Postgraduate Program
Ponte CMM [27]	Federal University of Pará	Master's Thesis	Public Health
Soares LR [28]	University of São Paulo	Master's Thesis	Experimental Pathophysiology
Freitas E [29]	Catholic University of Santos	Master's Thesis	Public Health

Table 2: Quality criteria of the studies included in the review.

indicates the universities in which the theses and dissertations were defended.

Synthesis of results

The prevalence of lipodystrophy in people living with HIV ranged between 32.4% [24] and 88.6% [30]. The weighted average of lipodystrophy among the 5,834 participants was 53.4% (in some studies part of the sample was excluded from the analysis of lipodystrophy). With regard to lipodystrophy classification, there was a 32.7% prevalence of lipohypertrophy, ranging from 12.1% [26] to 49.2% [17], 43.7% prevalence of lipoatrophy, ranging from 7.5% [30] to 53.2% [31], and 33.8% prevalence of mixed lipodystrophy, ranging from 14.4% [28] to 46.7% [30] in the studies that had provided this information (Table 1).

Patient self-report on changes in body-fat distribution after HIV infection diagnosis associated with clinician examination was the most common method of lipodystrophy assessment in the studies reviewed (n=6) [18,19,23,26-28] and that showed the greatest variation in prevalence rates, from 38.5% [26] to 67.9% [19]. Other methods used for lipodystrophy diagnosis in these studies were patient self-report alone (n=4) [17,20,21,28]; clinician diagnosis associated with body measurements (n=1) [22]; patient self-report associated with body measurements (n=2) [30,31]; and clinician diagnosis alone (n=2) [24,25].

Discussion

The estimation of prevalence and incidence of HIV-associated lipodystrophy is somewhat complex because there is no universal consensus on the diagnostic criteria. Furthermore, there are differences in establishing diagnostic criteria for lipodystrophy and lipoatrophy and how the outcome is described in the literature.

According to the studies reviewed, the prevalence of lipodystrophy was quite variable among people living with HIV. This variability can be explained by the heterogeneity of the different methods that were used for the diagnosis of HIV-associated lipodystrophy, due to the small sample size and the use of non-probability samples in some studies.

Comparing our data with reports from international studies, it was found that prevalence of lipodystrophy may range between 2% and 84%, depending on the criteria used for its detection [12,32], and this is

due to the use of different methods to assess lipodystrophy and a lack of standard diagnostic criteria available for clinical practice [33].

So far, there is no consensus or reference method for the diagnosis of HIV-associated lipodystrophy, and researchers use different methods for case definition, which implies variations in prevalence rates, as well as difficulty to determine etiology and treatment of lipodystrophy in people living with HIV [5,6,12]. Current diagnostic methods include patient self-assessment, physician assessment, anthropometric measurements and imaging studies [6,12,34].

Anthropometric indicators of body-fat as the sum of skinfold thicknesses, waist/hip ratio and waist circumference are used to detect alterations caused by HIV infection or triggered by HAART. However, there is no uniform standardization regarding the cutoff points that should be used to define such increase or decrease in body-fat measurements, taking into account individual characteristics, either currently or previously to HIV infection. Whereas anthropometric measurements are more objective than clinical assessment, they are more limited because there is no measurement standardization. Facial lipoatrophy, for example, even being one of the landmarks of the morphological changes described in HIV-infected population, does not have standardized measurement units [33]. In addition, the use of anthropometric measurements requires intense training and standardization sessions [34].

Imaging tests such as ultrasound, dual-energy X-ray absorptiometry (DEXA), computed tomography (CT) and nuclear magnetic resonance imaging are also used in the diagnosis of HIV-associated lipodystrophy. However, they are high-cost and difficult to access in the public health care system [3,18,35]. In addition, DEXA and CT pose a risk of radiation exposure and the risks and benefits to individuals living with HIV should be considered, as patients have to undergo these radiation exams numerous times for clinical follow-up [35,36].

Diagnostic method based on the presence of symptoms subjectively reported by the patient together with clinical examination is commonly used to determine the prevalence of lipodystrophy in HIV infection, both in research studies and in clinical practice, because it is low-cost and easy to implement. This method allows the report of noticeable changes in body-fat distribution that may occur concomitantly to HAART [17,18,23,28]. Nonetheless, it should be highlighted that it is a subjective method depending on patient self-reported, and would

require medical supervision during the whole time to ensure reliability and accuracy of information. In addition, there are no standard criteria specific for clinical examination. The Brazilian Ministry of Health accepts the definition of lipodystrophy self-reported by the patient and confirmed by medical examination [37].

In the studies reviewed, although the method used for the diagnosis of lipodystrophy was mentioned, there was little or no description of case definition adopted to determine the prevalence of lipodystrophy in people living with HIV. The cut-off points were not indicated when using objective measurements and there was no detail on how self-reported data were analyzed. This lack of information often impairs reproducibility of the study or data comparison.

Changes in body-fat distribution and metabolic changes in individuals living with HIV are among the leading complications resulting from HAART. Protease inhibitors and reverse transcriptase inhibitors, two major components of HAART regimens, have been implicated as the cause of HIV-associated lipodystrophy, as well as the time of exposure to HAART [5-7,10,13]. Ceccato et al. [24] investigated the association between the incidence of lipodystrophy and dyslipidemia and the longer use of protease inhibitors. Signorini et al. [27] evaluated the content of body-fat in HIV-infected individuals according to the duration of HAART, and found that all patients had lipodystrophy after one year of HAART. On the other hand, no patient with less than one year of pharmacological treatment had lipodystrophy. Studies have reported the association between lipodystrophy incidence and long-term antiretroviral therapy [18,23,28-30].

Nonetheless, changes in body-fat distribution have been reported in HIV-infected individuals who were not on HAART. In the study by Diehl et al. [18], lipodystrophy was observed in 27% of individuals living with HIV who had never used HAART. Some studies have shown that patients with longer HIV infection and exposed to HAART had higher prevalence of lipodystrophy than their counterparts [17,18,23,24,28,29].

Not all the surveyed patients developed lipodystrophy associated with HIV [17-31], which suggests that lipodystrophy syndrome varies not only with respect to the length of time of the treatment regimen, but also in relation to the effects of systemic chronic inflammatory process resulting from HIV infection itself and factors associated with lifestyle such as physical activity, dietary pattern, and other factors [23,36,37]. There are few studies in the literature comparing these changes with those of non-HIV-infected individuals, because a fat gain can happen with natural aging, or as an immune recovery process after initiation of HAART regimen [38,39].

Besides physical problems, HIV-associated lipodystrophy can generate psychological and social problems [15], arising from the dissatisfaction with body image [29], as well as induce treatment discontinuation.

Limitations of this study include methodological heterogeneity in the diagnosis of lipodystrophy and the sample size which may be insufficient to ensure the external validity of prevalence rates. In addition, the lack of data on confidence intervals prevented the summarization of data through meta-analysis. Because HIV-associated lipodystrophy has only been observed over recent years, there are few published works on the subject. That is why we decided to include all studies published and relevant to our aim in our review. On average, the published works revealed intermediate-to-high-quality data, according to our assessment.

Based on our review, we found that the prevalence of lipodystrophy was 53.5% among people living with HIV in Brazil. Patients self-report confirmed by physician examination was the most commonly used method for lipodystrophy assessment.

Further longitudinal studies should be conducted to determine the incidence of lipodystrophy, as well as diagnostic studies to determine high-sensitivity measurement methods, in accordance with the definition of lipodystrophy.

Awareness of the prevalence of HIV-associated lipodystrophy is an important planning tool to implement health care services directed to individuals with HIV-associated lipodystrophy, in the prevention and treatment of this condition.

References

1. World Health Organization (2008) World health statistics 2008. Geneva, WHO.
2. Palella FJ Jr, Delaney KM, Moorman AC, Loveless MO, Fuhrer J, et al. (1998) Declining morbidity and mortality among patients with advanced human immunodeficiency virus infection. HIV Outpatient Study Investigators. *N Engl J Med* 338: 853-860.
3. Valente AM, Reis AF, Machado DM, Succi RC, Chacra AR (2005) Metabolic alterations in HIV-associated lipodystrophy syndrome. *Arq Bras Endocrinol Metabol* 49: 871-881.
4. Martinez E, Mocroft A, Garcia-Viejo MA, Pérez-Cuevas JB, Blanco JL, et al. (2001) Risk of lipodystrophy in HIV-1-infected patients treated with protease inhibitors: a prospective cohort study. *Lancet* 357: 592-598.
5. Batterham MJ, Garsia R, Greenop PA (2000) Dietary intake, serum lipids, insulin resistance and body composition in the era of highly active antiretroviral therapy 'Diet FRS Study'. *AIDS* 14: 1839-1843.
6. Bedimo RJ (2008) Body-fat abnormalities in patients with HIV: progress and challenges. *J Int Assoc Physicians AIDS Care (Chic)* 7: 292-305.
7. Carr A, Samaras K, Chisholm D, Cooper DA (1998) Pathogenesis of HIV-1-protease inhibitor-associated peripheral lipodystrophy, hyperlipidaemia, and insulin resistance. *Lancet* 351: 1881-1883.
8. Rodrigues RL, Domingos H, Cunha RV, Paniago AM, Souza AS (2009) Risco cardiovascular pré e pós- terapia antirretroviral potente nos pacientes com síndrome da imunodeficiência adquirida. *Rev Bras Clin Med* 7: 153-160.
9. Rezaee F, Dashty M (2013) Role of adipose tissue in metabolic system disorders adipose tissue is the initiator of metabolic diseases *J Diabetes Metab S13*: 008..
10. Lichtenstein KA (2005) Redefining lipodystrophy syndrome: risks and impact on clinical decision making. *J Acquir Immune Defic Syndr* 39: 395-400.
11. Baril JG, Junod P, Leblanc R, Dion H, Therrien R, et al. (2005) HIV-associated lipodystrophy syndrome: A review of clinical aspects. *Can J Infect Dis Med Microbiol* 16: 233-243.
12. Carr A (2003) HIV lipodystrophy: risk factors, pathogenesis, diagnosis and management. *AIDS* 17 Suppl 1: S141-148.
13. Louie M, Markowitz M (2002) Goals and milestones during treatment of HIV-1 infection with antiretroviral therapy: a pathogenesis-based perspective. *Antiviral Res* 55: 15-25.
14. Collins E, Wagner C, Walmsley S (2000) Psychosocial impact of the lipodystrophy syndrome in HIV infection. *AIDS Read* 10: 546-550.
15. Sanches RS, Mill J, Machado AA, Donadi EA, Morais Fernandes AP (2009) Facial lipodystrophy: appearances are not deceiving. *J Assoc Nurses AIDS Care* 20: 169-175.
16. Malta M, Cardoso LO, Bastos FI, Magnanini MM, Silva CM (2010) STROBE initiative: guidelines on reporting observational studies. *Rev Saude Publica* 44: 559-565.
17. Santos CP, Felipe YX, Braga PE, Ramos D, Lima RO, et al. (2005) Self-perception of body changes in persons living with HIV/AIDS: prevalence and associated factors. *AIDS* 19 Suppl 4: S14-21.
18. Diehl LA, Dias JR, Paes AC, Thomazini MC, Garcia LR, et al. (2008) Prevalence of HIV-associated lipodystrophy in Brazilian outpatients: relation with metabolic

- syndrome and cardiovascular risk factors. *Arq Bras Endocrinol Metabol* 52: 658-667.
19. Monnerat BZ, Cerutti Junior C, Canicali SC, Motta TR (2008) Clinical and biochemical evaluation of HIV-related lipodystrophy in an ambulatory population from the Hospital Universitário Cassiano Antonio de Moraes, Vitória, ES, Brazil. *Braz J Infect Dis* 12: 364-368.
20. De Carvalho EH, Miranda Filho DB, Ximenes RA, Albuquerque MF, Melo HR, et al. (2010) Prevalence of hyperapolipoprotein B and associations with other cardiovascular risk factors among human immunodeficiency virus-infected patients in Pernambuco, Brazil. *Metab Syndr Relat Disord* 8: 403-410.
21. Arruda Júnior ER, Lacerda HR, Moura LC, Albuquerque Mde F, Miranda Filho Dde B, et al. (2010) Profile of patients with hypertension included in a cohort with HIV/AIDS in the state of Pernambuco, Brazil. *Arq Bras Cardiol* 95: 640-647.
22. Trinca JR, Sprinz E, Lazzaretti RK, Hutz MH, Kuhmmer R, et al. (2010) SNPs in the APM1 gene promoter are associated with adiponectin levels in HIV-infected individuals receiving HAART. *J Acquir Immune Defic Syndr* 55: 299-305.
23. Segatto AF, Freitas Junior IF, Santos VR, Alves KC, Barbosa DA, et al. (2011) Lipodystrophy in HIV/AIDS patients with different levels of physical activity while on antiretroviral therapy. *Rev Soc Bras Med Trop* 44: 420-424.
24. Ceccato MG, Bonolo PF, Souza Neto AI, Araújo FS, Freitas MI (2011) Antiretroviral therapy-associated dyslipidemia in patients from a reference center in Brazil. *Braz J Med Biol Res* 44: 1177-1183.
25. Gasparotto AS, Sprinz E, Lazzaretti RK, Kuhmmer R, Silveira JM, et al. (2012) Genetic polymorphisms in estrogen receptors and sexual dimorphism in fat redistribution in HIV-infected patients on HAART. *AIDS* 26: 19-26.
26. Signorini DJ, Monteiro MC, Andrade Mde F, Signorini DH, Eyer-Silva Wde A (2012) What should we know about metabolic syndrome and lipodystrophy in AIDS? *Rev Assoc Med Bras* 58: 70-75.
27. Signorini DJ, Oliveira Netto AM, Monteiro MC, Signorini DH, Codeço CT, et al. (2012) Differences in body fat distribution assessed by ultrasonography in patients receiving antiretroviral drugs. *Rev Assoc Med Bras* 58: 197-203.
28. Ponte CMM (2010) Distúrbios metabólicos associados à infecção pelo HIV/Aids: prevalência em pacientes ambulatoriais seguidos em hospital de referência do Estado do Ceará, Brasil [Dissertação]. Fortaleza (CE): Universidade Federal do Ceará, Programa de Pós-Graduação em Saúde Coletiva.
29. Soares LR (2010) Perfil antropométrico e distribuição da gordura corpórea relacionados ao risco cardiovascular em adultos vivendo com HIV/AIDS [Dissertação]. São Paulo (SP): Faculdade de Medicina da Universidade de São Paulo, Programa de Fisiopatologia Experimental.
30. Freitas E (2011) Prevalência de síndrome lipodistrófica em portadores do vírus da imunodeficiência humana (HIV-1/AIDS) com ou sem uso de Terapia Antirretroviral [Dissertação]. Santos (SP): Universidade de Católica de Santos, Programa de Mestrado em Saúde Coletiva.
31. Schuelter-Trevisol F, Alencastro PR, Ribeiro PAB, Wolff FH, Ikeda MLR, et al. (2012) Association of Physical Activity with Lipodystrophy Syndrome in HIV-Infected Patients. *J AIDS Clin Res* 3:177.
32. Peterson S, Martins CR, Cofrancesco J Jr (2008) Lipodystrophy in the patient with HIV: social, psychological, and treatment considerations. *Aesthet Surg J* 28: 443-451.
33. Tien PC, Grunfeld C (2004) What is HIV-associated lipodystrophy? Defining fat distribution changes in HIV infection. *Curr Opin Infect Dis* 17: 27-32.
34. Florindo AA, Latorre Mdo R, Santos EC, Borelli A, Rocha Mde S, et al. (2004) Validation of methods for estimating HIV/AIDS patients' body fat. *Rev Saude Publica* 38: 643-649.
35. Carr A (2007) Treatment strategies for HIV lipodystrophy. *Curr Opin HIV AIDS* 2: 332-338.
36. Brasil Ministério da Saúde (2008) Recomendações para terapia anti-retroviral em adultos infectados pelo HIV. Ministério da Saúde, Secretária de Vigilância em Saúde. Programa Nacional de DST, Aids.
37. Cofrancesco J Jr, Freedland E, McComsey G (2009) Treatment options for HIV-associated central fat accumulation. *AIDS Patient Care STDS* 23: 5-18.
38. Tien PC, Cole SR, Williams CM, Li R, Justman JE, et al. (2003) Incidence of lipoatrophy and lipohypertrophy in the women's interagency HIV study. *J Acquir Immune Defic Syndr* 34: 461-466.
39. Brown TT, Xu X, John M, Singh J, Kingsley LA, et al. (2009) Fat distribution and longitudinal anthropometric changes in HIV-infected men with and without clinical evidence of lipodystrophy and HIV-uninfected controls: a substudy of the Multicenter AIDS Cohort Study. *AIDS Res Ther* 6: 8.