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Lipodystrophy syndrome and cardiovascular risk factors in children and adolescents infected with HIV/AIDS receiving highly active antiretroviral therapy

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Abstract

Objective: To describe lipid profile, body shape changes, and cardiovascular risk factors in children and adolescents infected with HIV/AIDS receiving highly active antiretroviral therapy.

Methods: We investigated 43 children and adolescents being treated with this therapy at the outpatient clinic of pediatric infectious diseases of Instituto Fernandes Figueira/Fundação Oswaldo Cruz, Rio de Janeiro, Brazil. Values of total cholesterol, high-density lipoprotein, low-density lipoprotein, and triglycerides were determined. We also performed glucose tolerance test and analyzed body fat distribution, nutritional status, dietary intake, and family history of cardiovascular risk. The statistical analysis was performed using Student's *t* test. Significance level of p-value was lower than 0.05.

Results: We found lipid abnormality in 88.3% and body shape change in 13.9% of the cases. Nutritional status was adequate (81.3%) in most of the study population. Cholesterol intake in children older than 9 years was above the recommended value.

Conclusion: Prevalence of dyslipidemia and, therefore, risk for cardiovascular diseases were high during the use of highly active antiretroviral therapy.

J Pediatr (Rio J). 2010;86(1):27-32: Lipodystrophy, HIV, cardiovascular diseases, children, adolescents.

Introduction

The use of the highly active antiretroviral therapy (HAART) resulted in the decrease in the malnutrition and mortality associated with the acquired immune deficiency syndrome (AIDS) in developed countries and in Brazil in spite of the increase in the number of individuals with AIDS in developing countries.[1]

However, this type of treatment caused a metabolic complication called lipodystrophy syndrome (LDS), which is characterized by changes in body fat distribution (increased waist and breast measurements, accumulation of fat in the back of the neck and around the neck and jaws, thinness of the face, mainly the cheeks, and the buttocks) and/or metabolic abnormalities (insulin resistance and dyslipidemia),[2] which increase the risks for cardiovascular diseases.

Children with high serum levels of cholesterol are prone to have hypercholesterolemia in adulthood. Atherosclerotic plaques can be reversed in the beginning of their development.[3]

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Children infected with human immunodeficiency virus (HIV) are more vulnerable to the side effects of antiretroviral drugs since they need to be treated for decades, which leads to a cumulative exposure. On the other hand, drugs used to treat dyslipidemia have been rarely investigated in children, and some of them should be cautiously used because they affect the serum level of antiretroviral drugs.[4] In addition, the current epidemiological transition suggests that a diet rich in saturated fats associated with a sedentary lifestyle is a risk factor for cardiovascular diseases.

Nevertheless, we could not find data on the prevalence of LDS and cardiovascular risk factors in Brazilian children and adolescents infected with HIV/AIDS receiving the HAART regimen.

Therefore, based on the opportunity of treating this type of special patients at our service, the objective of the present study is to describe lipid profile, body shape changes and risk factors for cardiovascular diseases in children and adolescents infected with HIV/AIDS who were being treated with the HAART.

Methods

This is a descriptive cross-sectional study involving 43 carriers of HIV/AIDS. We conducted a survey including all patients between 2 and 16 years old with diagnosis of HIV who were treated from January to July 2004 at the outpatient clinic of pediatric infectious diseases of Instituto Fernandes Figueira/Fundação Oswaldo Cruz (IFF/Fiocruz), Rio de Janeiro, Brazil. Inclusion criteria were as follows: being older than 2 years and receiving stable treatment with HAART during at least 3 months before the beginning of the study. Those patients using medications that could interfere with the lipid and glucose profile, who did not comply with the treatment, and who had hypothyroidism were excluded. This sample is part of a cohort systematically followed up at IFF from the moment the disease was diagnosed. Considering a prevalence of 50% of dyslipidemia in patients with HIV, the number of patients analyzed provides 80% statistical power and 95% confidence interval.

Data regarding family history of risk of cardiovascular disease, disease classification, viral load and CD4 T-lymphocyte count (up to 3 months before and after data collection), antiretroviral drugs used and stage of sexual maturity (SSM) according to Tanner's classification were collected.[5]

Nutritional status was classified according to the body mass index (BMI) for age and sex.[6] Tricipital skinfold (TSF) and subscapular skinfold (SSF) were measured to assess changes in body fat distribution according to Frisacho.[7]

Lipodystrophy was diagnosed based on the simultaneous presence of two criteria: patient's report and abnormalities detected by the physician during clinical examination. The following are the changes in body fat distribution taken into consideration: central lipohypertrophy (accumulation of fat in the trunk and/or abdomen, breast, or posterior cervical region – "buffalo hump") and SSF above the 90th percentile; peripheral lipoatrophy (reduction of adipose tissue in the face, anterior and lateral cervical region, lower and/or upper limbs or buttocks)[8] and TSK below the 5th percentile; or mixed lipodystrophy (both conditions at different levels).

The antiretroviral drugs used were: nucleoside analogue reverse transcriptase inhibitors (NRTIs) (zidovudine, didanosine, lamivudine, stavudine), nonnucleoside analogue reverse transcriptase inhibitors (NNRTIs) (efavirenz) and protease inhibitors (PIs) (nelfinavir, ritonavir, lopinavir/ritonavir). We considered a medication regimen with PI (PI + NRTI; PI + NRTI + NNRTI) and without PI (NRTI + NNRTI).

Laboratory tests were carried out after a 12-hour fasting. The tests of total cholesterol, HDL-cholesterol (HDL-c), triglycerides (TG) and glycemia were performed using the enzymatic method according to the parameters of the 1st Guideline of Prevention of Atherosclerosis in Children and Adolescents.[9] The LDL-cholesterol (LDL-c) was calculated using the Friedewald formula. The oral glucose tolerance test (OGTT) was carried out after administration of dextrose (1.75 g/kg).[10]

Physical activities refer to the daily frequency during the 6 months before the study. The family history of risk for cardiovascular disease was assessed according to the criteria of the American Heart Association (AHA).[11]

The semiquantitative food frequency questionnaire adapted and used for dietary intake was analyzed using the computer program NutWin – Programa de Apoio à Nutrição, version 1.5 of Universidade Federal de São Paulo, Escola Paulista de Medicina (UNIFESP-EPM), São Paulo, state of São Paulo, Brazil.

Fat intake was measured based on the recommendations of the AHA[11] and, for carbohydrate, we considered the values between 55 and 60% of the total energy value. Energy requirements and fiber intake were measured according to the recommendations of the Dietary Reference Intakes.[12] Energy consumption was considered adequate when it reached 120% of the recommended value for sex and age.[13]

Data were stored and analyzed using the computer program Epi-Info, version 6.04. The statistical analyses were conducted using measurements of central tendency and variability. The continuous variables were tested in terms of distribution of normality; Student's *t* test was used to assess the difference between the continuous variable associated with the outcome. Significance was defined as p value less than 0.05.

The research project was approved by the Research Ethics Committee of IFF/Fiocruz.

Results

The general characteristics of the population studied are shown in Table 1. Of the 43 patients, 24 were children (6.70±2.05 years) and 19 were adolescents (13.21±1.81 years). Their age ranged from 2 to 16 years old, 51.2% were male and 48.8% were female, and in 95.4% of the cases there was vertical infection.

Approximately 81.3% of the patients had an adequate nutritional status; 23.3% of them had low height, and eight were older than 10 years. Of the 11.6% who had low weight, only one had TSK below the 5th percentile. The child who had SSF above the 90th percentile was overweight.

Among the adolescents, 21% were at pre-puberty (SSM1); 36.8% were classified as SSM2; 31.6% were SSM3; 5.3% were SSM4; and 5.3% were SSM5. Changes in body fat distribution were found in 13.9% of the population studied, with 9.3% of lipoatrophy and 4.7% of lipohypertrophy. All of them had serum lipid abnormality (50% had abnormal TG values; 16.6% had high levels of LDL-c; 33.3% had abnormal total cholesterol values; and 66.6% had high levels of HDL-c). Combined abnormality was not found. We found two patients with lipohypertrophy showing a SSF above the 90th percentile, and only one patient was overweight. Four patients had TSK below the 5th percentile and adequate nutritional status.

We found abnormal levels of total cholesterol, LDL-C, HDL-c, and TG in 32.6, 21.4, 79.1, and 30.2% of the cases, respectively. None of the patients had abnormal results on the OGTT. Our results showed that 88.3% of the population studied had serum lipid abnormality.

The absence of an LDL-c value was due to the presence of a TG value higher than 400 mg/dL; two patients did not undergo the OGTT: one of them because of vomiting after taking dextrose and the other one was not available for the second blood collection.

The association between time of antiretroviral drug use and concentration of serum lipids and body fat distribution did not show a significant statistical difference in the bivariate analyses; therefore, a multivariate model was not created. Nevertheless, those patients who used medication for a longer period of time had abnormal LDL-c fraction (Table 2).

In terms of dietary intake, we found an energy intake above 120% of the recommended values in 53.5% (n = 23) of the sample. The population studied included only one 2-year-old child whose dietary intake was in agreement with the recommendations for age and sex.

All male children between 3 and 8 years old had the carbohydrate percentage above the recommended value and the lipid intake was below the adequate values set by the AHA.[11] Cholesterol intake above 300 mg/day and fiber intake below the recommended value was found in the age group older than 9 years old. An inadequate energy intake was found in boys older than 14 years old (Table 3).

Table 1 - Characteristics of the population of children and adolescents infected with HIV/AIDS, Instituto Fernandes Figueira/ Fundação Oswaldo Cruz, 2004

Characteristics	n (%)
Type of medication	
With PI	36 (83.7)
Without PI	7 (16.3)
Viral load	
< 80 copies/mL	6 (13.9)
> 80 copies/mL	37 (86.1)
> 80 copies/mL*	12,000
CD4 (cells/mm^3)†	831.04±496.27
Disease classification	
A1	3 (7.0)
A2	3 (7.0)
A3	1 (2.3)
B1	4 (9.3)
B2	6 (14.0)
B3	9 (20.9)
C1	2 (4.6)
C2	2 (4.6)
C3	13 (30.2)
Family history of risk for cardiovascular disease	
Yes	29 (67.4)
No	2 (4.6)
Does not know	12 (27.9)

AIDS = acquired immune deficiency syndrome; HIV = human immunodeficiency virus; PI = protease inhibitors.
* Median.
† Mean ± standard deviation.

Table 2 - Association between time of antiretroviral drug use and concentration of serum lipids and body fat distribution in children with HIV/AIDS, Instituto Fernandes Figueira/Fundação Oswaldo Cruz, 2004

n (%)	Time of drug use (years)*	p	
Serum lipids			
Total cholesterol (n = 43)			
Abnormal	14 (32.6)	3.92±1.49	
Normal	29 (67.4)	3.31±1.63	0.71
LDL-c (n = 42)			
Abnormal	09 (21.4)	4.00±1.32	
Normal	33 (78.6)	3.38±1.65	0.45
HDL-c (n = 43)			
Abnormal	34 (79.1)	3.53±1.54	
Normal	09 (20.9)	3.44±1.88	0.47
Triglycerides (n = 43)			
Abnormal	13 (30.2)	3.61±1.80	
Normal	30 (69.8)	3.46±1.52	0.47
Body fat distribution			
Lipoatrophy (n = 43)			
Present	04 (13.9)	2.75±1.70	
Absent	37 (86.1)	3.59±1.58	0.86
Lipohypertrophy (n = 43)			
Present	02 (4.7)	3.50±2.12	
Absent	41 (95.3)	3.51±1.59	0.70

AIDS = acquired immune deficiency syndrome; HIV = human immunodeficiency virus.
* Mean ± standard deviation.
p associated with Student's *t* test.

Table 3 - Intake of energy, total lipids, saturated fatty acids, cholesterol and fibers in children and adolescents infected with HIV/AIDS, Instituto Fernandes Figueira/Fundação Oswaldo Cruz, 2004

	Calories (kcal)	CH (%)	Lipid (%)	Cholesterol (mg)	SFA (%)	Fiber (g)
3 to 8 years						
Male (n = 11)	2615.86±601.65	62.62±3.32	24.55±2.97	223.56±89.03	6.96±1.95	27.72±8.34
Female (n = 6)	2140.67±427.93	58.31±2.70	27.65±3.77	250.84±53.88	8.15±2.08	23.81±6.54
9 to 13 years						
Male (n = 6)	2517.50±694.32	58.50±4.38	27.40±3.39	349.56±103.08	8.27±1.26	20.40±4.34
Female (n = 9)	2665.40±576.28	55.50±4.91	29.80±4.08	366.41±159.42	8.77±2.33	20.37±7.07
14 to 18 years						
Male (n = 5)	2691.80±751.91	60.93±6.55	25.36±5.32	305.66±62.91	8.01±1.78	24.82±3.88
Female (n = 5)	2665.40±576.28	58.51±4.54	28.68±3.80	305.26±83.52	8.05±0.71	25.90±3.32

AIDS = acquired immune deficiency syndrome; CH = carbohydrate; HIV = human immunodeficiency virus; SFA = saturated fatty acids.

Regular physical activity was reported only by three children. On the other hand, sedentary activity (TV or electronic games) for longer than 2 hours a day was reported by 62.5% of the population (n = 40).

Discussion

Most of the sample studied had adequate nutritional status, both according to BMI and body composition based on TSK. Such finding is in agreement with a prospective study conducted with children according to which, after the regression model analysis, the therapy with PI improved weight, weight/height, and upper-arm circumference, with significant increased weight since the first assessments.[14]

However, a retrospective study found an increase in weight and height after the use of HAART without changes in the BMI.[15]

The low height found in the adolescents included in the present study may have been caused by the longer exposure to HIV before the HAART started to be used.

Before the HAART era, linear growth and weight gain were hardly maintained in children infected with HIV.[16] On the other hand, after the antiretroviral drugs started to be used, the weight usually improves during the first year, and the height usually improves after the second year.[17]

The high prevalence of dyslipidemia (88.3%) found in the present study is above the rate found in the literature.[8,18,19] This may have been caused by the fact that the references used for the analysis of serum lipids had a higher cutoff point. Nevertheless, this prevalence of dyslipidemia may also be a consequence of HIV infection itself. Increased TG serum levels have been reported in the literature before the HAART era and sometimes they may occur during the transition to AIDS.[20] In the present study, we found that 30.2% of the population had a disease classification with severe depletion of the clinical and immunological status (C3). However, it was not possible to relate it to the lipid abnormalities.

The association between time of antiretroviral drug use and serum lipid level did not show a significant statistical difference probably due to the small number of patients. Nevertheless, a retrospective study involving children infected with HIV during the perinatal period found abnormal cholesterol levels when the median of time of drug use was 1.61 and 4.65 years for values higher than 180 and 200 mg/dL, respectively, regardless of the treatment with the HAART.[21] A study with 21 patients from 1 to 17 years old who were infected with HIV and treated with PI found that 12 patients who used ritonavir or nelfinavir had abnormal total cholesterol and TG values.[22] On the other hand, another study with children and adolescents treated with NRTI combined with PI (nelfinavir and ritonavir), or without PI, showed high levels of total cholesterol, LDL-c and TG in those patients treated with PI, but the HDL-c values did not show any differences between the groups.[23] Our findings showed that 83.7% of the children and adolescents used PI (nelfinavir and ritonavir). However, since most of them used nelfinavir, we could not investigate the association between the metabolic abnormality and these inhibitors.

In spite of the high prevalence of abnormal HDL-c fraction, it is not possible to confirm that there was only a drug influence because of the trend of a sedentary lifestyle found in the population studied, since this is also a cardiovascular risk factor during childhood and adolescence.[24] Such result reinforces the importance of physical activity according to the recommendations of the National Cholesterol Education Program (NCEP),[25] mainly in this population of patients with HIV due to the other risks for cardiovascular diseases.

All patients had normal values on the OGTT. This may be due to the fact that in the present study most adolescents were at pre-puberty and, according to Jaquet et al.,[8] impaired glucose tolerance and reduced insulin sensitivity develop during puberty. Another possible explanation for such result is that insulin resistance may be caused by some antiretroviral drugs such as indinavir (PI),26 which was not used by the population included in our study.

The change in body fat distribution was less prevalent than the serum lipid abnormalities. This suggests that dyslipidemia occurs before body shape changes, which is in agreement with the data found by another study.[8] The low prevalence of body shape changes we found is different from the rates found in other studies.[18,27] This may be a result of the different diagnostic criteria used in the studies. In addition, such data are difficult to investigate due to the changes in body fat distribution that take place during childhood and adolescence.

A study using the dual energy X-ray absorptiometry (DEXA) detected changes in body composition even in the absence of changes in body fat distribution.[28] However, in the clinical practice, due to high costs and exposure to radiation, this exam is not recommended. Therefore, the measurement of skinfolds, an inexpensive and easy to perform technique, is more often used based on the assumption that the subcutaneous fat layer reflects the total body fat.

Even though most of the patients in our study were eutrophic, they had an energy intake higher than the recommended value, which suggests an increased energy demand in these patients. A study conducted with the objective of analyzing the macronutrient intake of children infected with HIV between 1995 and 2004 revealed that the calorie intake in the beginning of the study, before the HAART started to be used, was higher than the recommended values and that, these values were reduced later although they remained higher than the recommended values up to the end of the study.[29]

Our results revealed a high cholesterol intake in the age group older than 9 years old. One of the possible explanations for such phenomenon is that adolescents consume a greater amount of fat from food rich in cholesterol and saturated fat.

A systematic review of the literature evidenced no correlation between dietary intake and profile abnormality in patients infected with HIV who were using antiretroviral drugs. Such a finding may be a consequence of the different methods used in the studies.[30]

The fiber intake found in those patients older than 9 years old was below the recommended value for their age, and this was another factor contributing to the increase in the level of serum cholesterol, since, once fibers reach the bowels, they can attach to certain substances, such as cholesterol, reducing their absorption. The influence of the eating habits on metabolic complications associated with HIV infection has not been widely studied. However, the AIDS Clinical Trial Group panel recommends the use of the NCEP guideline, which suggests a diet including low saturated fat content and large amounts of fiber, maintenance of adequate body weight and increased practice of physical

activity for the treatment of dyslipidemia.[25] Such treatment is difficult to be used with adults with HIV, and there are limited data available on the use of statins in children. Furthermore, its use associated with certain antiretroviral drugs is contraindicated because, when it interferes with cytochrome P450, it leads to an inadequate suppression of the viral load or to a higher drug toxicity.[4]

The high frequency of family history of risk for cardiovascular disease is an important aspect because the genetic factors are influenced by the risk factors for atherosclerosis present during childhood and are difficult to be detected.

In conclusion, this population had lipodystrophy with high prevalence of dyslipidemia and, as a consequence, high risk for cardiovascular diseases in those children who were being treated with the HAART. However, due to the shortage of Brazilian studies involving this population, longitudinal studies are needed so that a better assessment of the cause-effect relation of such drugs can be achieved. Since the atherosclerotic disease has its onset during childhood, changes in eating habits and lifestyle with regular practice of physical exercises should be reinforced in this group of patients as part of their treatment.

References

1. World Health Organization. Weekly Epidemiological Record [website]. Global situation of the HIV/AIDS pandemic. 2003;50:425-32. http://www.who.int/wer/2003/en/wer7850.pdf. Access: 06/07/2004.
2. Carr A, Samaras K, Chisholm DJ, Cooper DA. Pathogenesis of HIV-1-protease inhibitor-associated peripheral lipodystrophy, hyperlipidaemia, and insulin resistance. Lancet. 1998;351:1881-3.
3. McGill HC Jr, McMahan CA. Determinants of atherosclerosis in the young. Pathobiological Determinants of Atherosclerosis in Youth (PDAY) Research Group. Am J Cardiol. 1998;82:30T-36T.
4. Leonard EG, McComsey GA. Metabolic complications of antiretroviral therapy in children. Pediatr Infect Dis J. 2003;22:77-84.
5. Tanner JM. Fetus into man-physical growth from conception to maturity. Cambridge: Harvard University Press; 1990.
6. Centers for Disease and Prevention. [website] CDC Growth Charts. http://www.cdc.gov/growthcharts. Access: 03/09/2003.
7. Frisancho AR. New norms of upper limb fat and muscle areas for assessment of nutritional status. Am J Clin Nutr. 1981;34:2540-5.
8. Jaquet D, Lévine M, Ortega-Rodriguez E, Faye A, Polak M, Vilmer E, et al. Clinical and metabolic presentation of the lipodystrophic syndrome in HIV-infected children. AIDS. 2000;14:2123-8.
9. Giuliano IC, Caramelli B, Pellanda L, Duncan B, Mattos S, Fonseca FH. I diretriz de prevenção da aterosclerose na infância e na adolescência. Arq Bras Cardiol. 2005;supl 6:3-36.
10. Miller O. Laboratório para o clínico. Rio de Janeiro: Atheneu; 1995.
11. Williams CL, Hayman LL, Daniels SR, Robinson TN, Steinberger J, Paridon S, et al. Cardiovascular health in childhood: A statement for health professionals from the Committee on Atherosclerosis, Hypertension and Obesity in the Young (AHOY) of the Council on Cardiovascular Disease in the Young, American Heart Association. Circulation. 2002;106:143-60.
12. Institute of Medicine. Dietary Reference Intakes for Energy, Carboydrates, Fiber, Fat, Fatty Acids, Cholesterol, Proteins, and Amino Acids (macronutrients). Washington: National Academy Press; 2002.
13. World Health Organization (WHO). Nutrient requirements for people living with HIV/AIDS: report of a technical consultation. Geneva: WHO; 2003.
14. Miller TL, Mawn BE, Orav EJ, Wilk D, Weinberg GA, Nicchitta J, et al. The effect of protease inhibitor therapy on growth and body compositions in immunodeficiency virus type-1 infected children. Pediatrics. 2001;107:E77.
15. Guillén S, Ramos JT, Resino R, Bellón JM, Muñoz MA. Impact on weight and height with the use of HAART in HIV-infected children. Pediatr Infect Dis J. 2007;26:334-8.
16. Fiore P, Donelli E, Boni S, Pontali E, Tramalloni R, Bassetti D. Nutritional status changes in HIV-infected children receiving combined antiretroviral therapy including protease inhibitors. Int J Antimicrob Agents. 2000;16:365-9.
17. Nachman SA, Lindsey JC, Moye J, Stanley KE, Johnson GM, Krogstad PA, et al. Growth of human immunodeficiency virus-infected children receiving highly active antiretroviral therapy. Pediatr Infect Dis J. 2005;24:352-7.
18. Sarni RO, de Souza FI, Battistini TR, Pitta TS, Fernandes AP, Tardini PC, et al. Lipodystrophy in children and adolescents with acquired immunodeficiency syndrome and its relationship with the antiretroviral therapy employed. J Pediatr (Rio J). 2009;85:329-34.
19. Tassiopoulos K, Williams PL, Seage GR 3rd, Crain M, Oleske J, Farley J, et al. Association of hypercholesterolemia incidence with antiretroviral treatment, including protease inhibitors, among perinatally HIV-infected children. J Acquir Immune Defic Syndr. 2008;47:607-14.
20. Salas-Salvadó J, García-Lorda P. The metabolic puzzle during the evolution of HIV infection. Clin Nutr. 2001;20:379-91.
21. Kim JY, Zaoutis T, Chu J, Zhao H, Rutstein R. Effects of highly active antiretroviral therapy (HAART) on cholesterol in HIV-1 infected children: a retrospective cohort study. Pharmacoepidemiol Drug Saf. 2009;18:589-94.
22. Temple ME, Koranyi KI, Nahata MC. Lipodystrophy in HIV-infected pediatric patients receiving protease inhibitors. Ann Pharmacother. 2003;37:1214-8.
23. Lainka E, Oezbek S, Falck M, Ndagijimana J, Niehues T. Marked dyslipidemia in human immunodeficiency virus-infected children on protease inhibitor-containing antiretroviral therapy. Pediatrics. 2002;110:e56. http://pediatrics.aappublications.org/cgi/content/full/110/5/e56. Access: 02/03/2004.
24. dos Santos MG, Pegoraro M, Sandrini F, Macuco EC. Fatores de risco no desenvolvimento da aterosclerose na infância e adolescência. Arq Bras Cardiol. 2008;90:301-8.
25. Dubé MP, Stein JH, Aberg JA, Fichtenbaum CJ, Gerber JG, Tashima KT, et al. 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. Clin Infect Dis. 2003;37:613-27.
26. Murata H, Hruz PW, Mueckler M. The mechanism of insulin resistance caused by HIV protease inhibitor therapy. J Biol Chem. 2000;275:20251-4.
27. Desai N, Mullen P, Mathur M. Lipodystrophy in pediatric HIV. Indian J Pediatr. 2008;75:351-4.
28. Viganò A, Mora S, Testolin C, Beccio S, Scheneider L, Bricalli D, et al. Increased lipodystrophy is associated with increased exposure to highly active antirretroviral therapy in HIV-infected children. J Acquir Immune Defic Syndr. 2003;32:482-9.
29. Sharma TS, Kinnamon DD, Duggan C, Weinberg GA, Furuta L, Bechard L, et al. Changes in macronutrient intake among HIV-infected children between 1995 and 2004. Am J Clin Nutr. 2008;88:384-91.
30. Almeida LB, Giudici KV, Jaime PC. Consumo alimentar e dislipidemia decorrente da terapia antirretroviral combinada para infecção pelo HIV: uma revisão sistemática. Arq Bras Endocrinol Metab. 2009;53:519-27.

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