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Central obesity and dietary intake in HIV/AIDS patients

Obesidade abdominal e consumo alimentar em portadores de HIV/Aids

ABSTRACT

OBJECTIVE: To assess the association between dietary intake and central obesity among people living with HIV/AIDS and receiving highly active antiretroviral therapy.

METHODS: A cross-sectional study was conducted involving 223 adult individuals in the city of São Paulo city in 2002. The study population was classified according to central obesity, defined as waist-to-hip ratio >0.95 for men and >0.85 for women. The dietary variables studied were energy consumption (in calories and calories/kilo of body weight), macronutrients (in grams and % of energy intake), total fiber (grams) and fruit and vegetables intake (grams). The potential confounders examined were sex, skin color, age, schooling, income, body mass index, physical activity, smoking habits, peripheral CD4+ T lymphocyte count and length of protease inhibitor use. The multiple logistic regression model was performed in order to evaluate the association between central obesity and dietary intake.

RESULTS: The prevalence of central obesity was 45.7% and it was associated with greater consumption of lipids: for every increase of 10g of lipid intake the odds of central obesity increased 1.28 times. Carbohydrate consumption showed negative association (OR=0.93) with central obesity after adjustment for control variables.

CONCLUSIONS: The results suggest that the amount of carbohydrates and lipids in the diet, regardless of total energy intake, may modify the chance of developing central obesity in the studied population. Nutritional interventions may be beneficial for preventing central obesity among HIV/AIDS patients.

KEYWORDS: Obesity. HIV-associated lipodystrophy syndrome. Anti-HIV agents, adverse effects. Food consumption. Dietary fats. Waist-hip ratio. Cross-sectional studies.

RESUMO

OBJETIVO: Avaliar a associação entre consumo alimentar e presença de obesidade abdominal em indivíduos infectados pelo HIV/Aids, em uso de terapia antiretroviral de alta potência.

MÉTODOS: Trata-se de estudo transversal envolvendo 223 indivíduos adultos, realizado no município de São Paulo, em 2002. A população de estudo foi classificada de acordo com a obesidade abdominal, definida pela razão das circunferências da cintura e quadril >0,95 para os homens e >0,85 para mulheres. As variáveis dietéticas estudadas foram consumo de energia (calorias e calorias/quilo de peso corporal), macronutrientes (em gramas e % da energia ingerida), fibra total (gramas) e consumo de frutas, verduras e legumes (gramas). Potenciais fatores de confusão examinados

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Received: 6/16/2005 Reviewed: 3/13/2006
Approved: 4/23/2006

foram sexo, raça, idade, escolaridade, renda, índice de massa corporal, nível de atividade física, tabagismo, contagem de linfócitos T CD4+ e tempo de uso de inibidor de protease. Estimou-se modelo de regressão logística para avaliar a relação entre obesidade abdominal e consumo alimentar.

RESULTADOS: A prevalência de obesidade abdominal foi de 45,7% e esteve associada ao maior consumo de lipídeos: para cada aumento de 10 g de lipídio na dieta a chance aumentou 1,28 vezes. O consumo de carboidratos mostrou-se negativamente associado (OR=0,93) com a presença de obesidade abdominal após ajuste pelas variáveis de controle.

CONCLUSÕES: Os resultados sugerem que a quantidade de carboidratos e lipídeos na dieta, independente do consumo energético, pode modificar a chance de desenvolver obesidade abdominal na população estudada. Intervenções nutricionais podem ser benéficas na prevenção de obesidade abdominal entre pacientes vivendo com HIV/Aids.

DESCRIPTORIOS: Obesidade. Síndrome de lipodistrofia associada ao HIV. Agentes anti-retrovirais, efeitos adversos. Consumo de alimentos. Lipídeos na dieta. Relação cintura-quadril. Estudos transversais.

INTRODUCTION

There has been great progress in the treatment of HIV/AIDS infection using medications, especially the use of highly active antiretroviral therapy (HAART) has ensured a significant increase in the survival of HIV-infected individuals in different regions around the world.^{3,19} The policy of universal free distribution of antiretroviral medications implemented in Brazil has ensured a notable increase in survival parallel to a reduction in the incidence of opportunistic infections and, consequently, a reduction in the rate of hospitalization among Brazilians living with HIV/AIDS.¹³

On the other hand, adverse events associated with therapy have been described among people living with HIV/AIDS and receiving highly active antiretroviral therapy, thereby placing new demands on the services providing integrated care for these patients. In this scenario, central obesity is a frequently morphological abnormality seen among both HIV-positive men and women.⁶

Central obesity is described as the presence of excess fat in the abdomen, out of proportion to total body fat, having three compartments: visceral, retroperitoneal, and subcutaneous.¹⁵ In healthy populations, it has now been showed that the deposition of abdominal fat is related to dietary intake, and it is an independent predictor of risk factors and morbidity.²² Waist-to-hip ratio has been used in a number of epidemiologic studies to show increased risk for diabetes, coronary artery disease, and hypertension. Nonetheless, waist circumference is the most practical anthropometric measurement for assessing abdominal fat.^{15, 21}

The present study focused on dietary components that had been identified in previous studies as determinants of metabolic syndromes and had been associated to the development of central obesity.^{9,11,22} The objective was to investigate the potential association of dietary components to the development of central obesity in people living with HIV/AIDS and receiving HAART. Therefore, there were examined the differences in dietary intake between individuals with and without abdominal fat deposition and the relationship between dietary components and central obesity.

METHODS

A cross-sectional study was conducted comprising individuals of both sexes aged between 20 and 59 years who had HIV/AIDS and had been using HAART with protease inhibitors for at least three years. They were being followed up at a reference service for the treatment of HIV/AIDS patients in the city of São Paulo, southeastern Brazil. This clinic is located in the central region of the city and accounts for outpatient follow-up of around 4,000 adult patients.

Recruitment for the study was carried out between March and June 2002 on the basis of consecutive sampling in accordance with patients' order of arrival for their periodic consultation with the clinic's infectious disease doctor. Patients were excluded from the study if they were undergoing treatment with corticoids, anabolic steroids or growth hormone; if they had had active opportunistic diseases (infections or tumors) in the three months prior to recruitment; or if they had gone through surgery such as liposuction or liposculpture during the six months prior to the

study. Pregnant women or using oral contraceptives were also excluded. Out of 276 patients invited to participate in the study, 27 refused (refusal rate of 9.4%) and 26 were excluded because of missing data from their medical records. Thus, the final sample comprised 223 patients.

Central obesity was defined as waist-to-hip ratio greater than 0.95 for men and 0.85 for women.²¹ The measurement of the waist-to-hip ratio has been validated for this sample of Brazilian HIV/AIDS patients and has good correlation with visceral fat ($r=0.74$; $p=0.009$) and total abdominal fat ($r=0.82$; $p=0.002$).⁴ Weight (kg) and height (m) were measured, and body mass indexes (BMI, in kg/m^2) were calculated according to the World Health Organization (WHO) criteria for classification.²² Peripheral subcutaneous fat was evaluated by means of the subscapular and triceps skinfolds (mm), taking the average of three measurements made using Lange skinfold calipers, which have a precision of 1.00 mm.

Current dietary intake was evaluated using two consecutive 24-hour dietary recall, excluding one weekend day. Each participant was interviewed twice. A nutritionist trained in the study protocol and using a standardized procedure instructed participants on how to describe their diet over the past 24-hour period. Once data was collected, food intake registered in the 24-hour dietary recall was converted into energy and nutrients by Virtual Nutri software* (version 1.0; Department of Nutrition, Universidade de São Paulo). The dietary variables studied were consumption of energy (in kcal and kcal/kg), macronutrients (in g and % of energy intake), total fiber, and fruit and vegetables (g). Macronutrient intake in grams (carbohydrates, proteins and lipids) was adjusted for total energy consumption using residual nutrient method.²⁰ In summary, this method allows to assessing the net effect of nutrients without the influence of energy intake.

In addition to dietary recall, participants answered two questionnaires. Questionnaire 1 collected data on personal identification, demographic and socioeconomic factors and smoking habit. These variables were self-reported information through the interviewer's guidance. Questionnaire 2 had to do with habitual physical activity. It consisted of 16 questions as a Likert scale and covered physical activity of the last 12 months by evaluating three components: occupational physical activity; physical exercise during leisure time; and leisure and locomotion activities. Each block of questions generated a final score for physical activity.⁵

The results from peripheral CD4+ T lymphocyte counts for each patient, performed by means of flow cytometry, were obtained from their respective medical records. Tests were performed no more than three months prior to the patient's admission to the present study. Likewise, the history of the prescribed antiretroviral medication was obtained, and the total length of protease inhibitor use (in months) was calculated.

Statistical analysis was performed using SPSS statistical software (version 10.0). The association between central obesity and demographic, clinical and anthropometric variables was assessed using the Chi-square test (categorical variables) and t-Student test (continuous variables).

A multiple logistic regression model was estimated in order to evaluate the association between central obesity and dietary intake, adjusting for potential confounders, such as sex, age, skin color (black or non-black), level of schooling (categories), income (in reais - R\$), BMI (kg/m^2), physical activity (score), smoking habits (yes/no), peripheral CD4+ T lymphocyte count (categories) and length of protease inhibitor use. The dependent variable was central obesity (yes/no) and dietary intake was the independent one. For energy and macronutrients it was estimated the change by 10 units and for the percentages of macronutrients in calories it was estimated the change by 1 unit. All dietary intake variables were analyzed as a continuous variable and a multiple model was estimated for each one.

This study was approved by the Institutional Review Board of the Faculdade de Saúde Pública and Faculdade de Medicina of Universidade de São Paulo, Brazil.

RESULTS

Of 223 individuals studied, the majority was male (76.8%). The average age was 38.9 years, ranging from 20 to 59 years.

The prevalence of central obesity was 45.7% (95% CI: 39.1-52.5%). The prevalence of underweight was greater among women than men, 7.7% and 2.3% respectively. Women also showed higher prevalence of central obesity and overweight when compared to men (Table 1).

Central obesity was greater among patients with less schooling and those having better peripheral CD4+ T lymphocyte counts. The length of protease inhibitor use was on average three months longer in the

*Virtual Nutrition software, version 1.0 [software em diskettes]. São Paulo: Departamento de Nutrição, Universidade de São Paulo; 1996.

Table 1 - Population characteristics (means and percentages) according to nutritional status and sex. São Paulo, Brazil, 2002.

Characteristic	Male (n=171)			Female (n=52)			p-value
	n	%	95% CI	n	%	95% CI	
Waist-to-hip ratio*							
Normal	99	57.9	50.1-65.4	22	42.3	28.7-56.9	0.048
Central obesity	72	42.1	34.6-49.9	30	57.7	43.2-71.3	
Body mass index*							
Underweight	4	2.3	0.6-5.9	4	7.7	2.1-18.5	0.063
Normal range	118	69.0	61.5-75.8	29	55.8	41.3-69.5	
Pre-obese	43	25.1	18.8-32.3	14	26.9	15.6-41.0	
Obese	6	3.5	1.3-7.5	5	9.6	3.2-21.0	

*Waist-to-hip ratio classification: central obesity greater than 0.85 for women and 0.95 for men.²²

**Body mass index classification: underweight (<18.5), normal range (18.5-24.9), overweight: pre-obese (25.0-29.9) and obese (≥30.0).²²

group with central obesity, but this difference was at the limit of statistical significance (p=0.06). Other selected characteristics are shown in Table 2.

The comparison of mean dietary intakes for patients with and without central obesity is presented in Table 3. Patients with central obesity had mean carbohydrate intake significantly lower than those without central obesity (53.6% vs 57.8%; p<0.01). The opposite was observed for fat intake, which was greater among those with central obesity (30.8 vs 27.7; p<0.01). There were no significant differences in protein, total fiber, and fruit and vegetable intake. After adjusting, energy for body weight (kcal/kg) intake was significantly lower among patients with abnormal abdominal fat redistribution (31.4 vs 35.3; p=0.04).

The results of the final logistic regression models for dietary variables are shown in Table 4. The effect of energy (kcal/kg) on the occurrence of abnormal fat redistribution was lost after adjusting for sex, age, skin color, schooling, income, BMI, physical activ-

ity, smoking habits and length of protease inhibitor use. Carbohydrate consumption showed negative association with central obesity. For every increase of 10 g of carbohydrates (value adjusted for energy), the odds of central obesity decreased 0.93 times, that is, 7%. On the other hand, a significant higher risk of central obesity was observed with greater lipid intake. For every increase of 10 g of lipids the odds increased 1.28 times. Considering the percent of energy intake, for every increase of 1 unit of lipids the odds of central obesity increased 1.07 times, after adjusting for control variables.

DISCUSSION

Redistribution of body fat has been increasingly recognized among HIV-infected individuals, and especially among those treated with protease inhibitors.^{1,2} In the present study, it was observed high prevalence of central obesity, and it was significantly greater among women than among men, and also among patients with less schooling. Previous studies^{6,14} on pa-

Table 2 - Population characteristics according to the presence of central obesity. São Paulo, Brazil, 2002.

Characteristic	Central obesity	
	Yes (n=102) n (%)	No (n=121) n (%)
Skin color		
Black	37 (44.0)	47 (56.0)
Non-black	65 (46.8)	74 (53.2)
Schooling*		
Up to 8 years	37 (52.9)	33 (47.1)
9-12 years	37 (51.4)	35 (48.6)
13 years or over	27 (34.2)	52 (65.8)
CD4+ cell count (cell/mm ³)**		
≤200	20 (48.8)	21 (51.2)
201-349	35 (34.0)	68 (66.0)
≥350	47 (59.5)	32 (40.5)
Smoking habits		
Yes	27 (39.7)	41 (60.3)
No	73 (48.4)	78 (51.6)
	Mean; Standard deviation	
Use of protease inhibitor (months)	34.1; 14.5	30.4; 14.3
Age (years)	41.6; 7.4**	37.0; 6.9
Physical activity (score)	2.75; 0.70	2.88; 0.65
Body mass index (kg/m ²)	25.6; 3.6**	22.2; 2.4
Waist circumference (cm)	93.1; 8.8**	80.6; 6.4
Hip circumference (cm)	95.0; 8.1**	91.2; 5.7
Waist-hip ratio	0.98; 0.1**	0.88; 0.1
Subscapular skinfold (mm)	25.5; 9.2*	17.6; 6.7
Triceps skinfold (mm)	9.8; 5.5	9.4; 4.7

**Statistically significant difference (Chi-square test for frequencies, Student's t-test for means): *p<0.05; **p<0.001.

Table 3 - Dietary intake of the population according to the presence of central obesity. São Paulo, Brazil, 2002.

Dietary variable	Central obesity (mean ± SD)		p-value**
	Yes (n=102)	No (n=121)	
Energy (kcal)	2,225.4±915.9	2,242.0±891.0	0.89
Energy/weight (kcal/kg)	31.4±12.8	35.3±14.0	0.04
Percentage of calories (%)			
Carbohydrates	53.6±10.6	57.8±10.0	<0.01
Proteins	16.1±4.3	15.4±5.3	0.32
Lipids	30.8±8.7	27.7±7.8	<0.01
Total carbohydrates (g)*	292.3±63.8	318.2±63.5	<0.01
Total proteins (g)*	88.8±24.8	85.9±32.6	0.46
Total lipids (g)*	80.1±22.9	70.8±22.4	<0.01
Total fiber (g)*	17.6±8.6	16.6±9.7	0.41
Total F&V (g)	236.0±202.2	259.3±262.9	0.48

*Nutrient intake adjusted for energy by using linear regression analysis

**Based on Student's t-test for means

tients treated with protease inhibitors have shown that the accumulation of fat is frequently greater among women and the development of android body patterns characterized by increase adiposity in the trunk has been reported among women with lipodystrophy.^{6,10}

The authors believe that it was correct to define cases of abdominal fat deposition by means of waist-hip ratio. Waist circumference and waist-hip ratio increase with the accumulation of visceral adiposity in individuals with or without HIV infection.^{4,12,21} Methods were validated for estimating body fat of these HIV/AIDS patients and visceral fat showed better correlation with the measurement of waist-hip ratio ($r=0.74$; $p=0.009$) than with the measurement of waist circumference ($r=0.60$; $p=0.050$).⁴ It was observed that the group of patients with central obesity presented significantly greater mean BMI, which is an indicator of total fat, and also significantly greater mean waist-hip ratio, waist circumference and subscapular skinfold, which are indicators of localized adiposity. On the other hand, there was no significant difference in the triceps skinfold between the two groups. This measurement is a parameter for evaluating lipodystrophy due to fat atrophy.

The redistribution of body fat is known to be multifac-

torial.²² Exposure to protease inhibitors and, more recently, to reverse transcriptase inhibitors has been implicated in the etiology of this morphological abnormality.^{2,7} It was observed that the length of protease inhibitor use was longer among patients with fat redistribution with a mean difference at the limit of statistical significance ($p=0.06$). In addition, it was noted that central obesity occurred more frequently in individuals with better response to antiretroviral therapy, as expressed by quantitative CD4+ T lymphocyte count, which is consistent with other reports.^{11,12}

The study findings suggest increased risk of central obesity when there is lower carbohydrate intake (OR=0.95) and greater lipid intake (OR=1.07), regardless of sex, age, skin color, schooling, income, BMI, physical activity, smoking habits and length of protease inhibitor use. On the other hand, other studies that have evaluated HIV-infected patients did not find an association between the intake of these macronutrients and fat deposition.^{1,9,11}

Individuals without central obesity presented greater mean energy intake per kg of body weight in the present study. This difference was also observed in a case-control study by Hendricks et al¹¹ for investigating the development of abdominal fat deposition in HIV-posi-

Table 4 - Association of dietary factors with the presence of central obesity. São Paulo, Brazil, 2002.

Dietary variables	β_k	OR _{aj} **	Change of odds
Per 1 unit			
Energy (kcal)	0.000	1.00 (1.00; 1.00)	-
Energy/weight (kcal/kg)	0.011	1.01 (0.98; 1.04)	-
Percentage of calories (%)			
Carbohydrates	-0.050	0.95 (0.92; 0.98)	-5%
Proteins	0.004	1.01 (0.94; 1.08)	-
Lipids	0.071	1.07 (1.02; 1.12)	+7%
Per 10 units			
Total carbohydrates (g)*	-0.007	0.93 (0.88; 0.98)	-7%
Total proteins (g)*	-0.001	0.99 (0.88; 1.11)	-
Total lipids (g)*	0.025	1.28 (1.06; 1.56)	+28%
Total fiber (g)*	0.004	1.04 (0.72; 1.51)	-
Total F&V (g)	-0.001	0.99 (0.97; 1.01)	-

*Nutrient intake adjusted for energy by using linear regression analysis

**Logistic regression model with central obesity as exposure variable adjusted for sex, age, skin color, schooling, income, body mass index, physical activity, smoking habits and length of protease inhibitor use (95% confidence interval between parentheses)

tive men. Since both body weight and BMI were significantly greater in the group with central obesity, it should be considered the possibility that there may have been underreporting of energy intake, as well documented previously among overweight individuals.^{8,18} In contrast, greater total energy intake was observed among patients with fat redistribution syndrome.¹

For protein, total fiber, and fruit and vegetable intake it was not found any differences in intake. A previous study identified that fiber-rich diets are negatively associated with fat deposition among HIV-infected individuals.¹¹ In a study of the relationship between modifiable dietary habits, central obesity and metabolic abnormalities, Hadigan et al⁹ observed that an increase of 5 g in the daily intake of fiber was associated with a 14% reduction in the area under the glycemic curve (insulin prediction area). However, there was no association with fat redistribution pattern. Dietary factors such as fiber intake may not be primary causes of morphological abnormalities but may be indirectly related to such abnormalities by means of their association with metabolic disturbances (hyperinsulinemia) that lead to the accumulation of abdominal fat.

The present study had some limitations. As it was a cross-sectional study focusing on abdominal fat deposition, the results may not be applicable to other patterns of

morphological abnormalities resulting from the use of protease inhibitors, such as fat atrophy. Nonetheless, when the study results are added to previous studies, they draw attention to the importance of healthy eating habits in determining whether lipodystrophy will occur or not. Moreover, it should be stressed that the use of nutritional therapy for HIV-infected patients has received little attention, even though many patients often express interest in this type of treatment.^{16,17}

Ensuring good quality of life for HIV-infected individuals in the era of HAART is also associated to preserving their corporal self-image, its physical aspects, and their self-esteem. Thus, the prevention of morphological abnormalities has an important role, not only from the point of view of reducing the metabolic risk and risk of future chronic diseases, but also for improving these patients' quality of life.

To that aim, follow-up and nutritional intervention studies are needed for evaluating the efficacy of nutritional therapy for modifying the risks of morphological and metabolic abnormalities associated with the use of antiretroviral therapy among HIV-infected patients. Once the efficacy of this type of intervention has been proven, it can be incorporated into the set of integrated health care actions available for people living with HIV/AIDS.

REFERENCES

- Batterham MJ, Garsia R, Greenop PA. Dietary intake, serum lipids, insulin resistance and body composition in the era of highly active antiretroviral therapy 'Diet FRS Study'. *Aids*. 2000;14:1839-43.
- Carr A, Samaras K, Thorisdottir A, Kaufmann GR, Chisholm DJ, Cooper DA. Diagnosis, prediction, and natural course of HIV-1 protease inhibitor associated lipodystrophy, hyperlipidaemia, and diabetes mellitus: a cohort study. *Lancet*. 1999;353:2093-9.
- Chen D, Misra A, Garg A. Lipodystrophy in human immunodeficiency virus-infected patients. *J Clin Endocrinol Metab*. 2002;87:4845-56.
- Florindo AA, Latorre MRDO, Santos ECM, Borelli A, Rocha MS, Segurado AAC. Validação de métodos de estimativa de gordura corporal em portadores do HIV/AIDS. *Rev Saúde Pública*. 2004;38:643-9.
- Florindo AA, Latorre MRDO, Santos ECM, Negrão CE, Azevedo LF, Segurado AAC. Validity and reliability of the Baecke questionnaire for the evaluation of habitual physical activity among people living with HIV/AIDS. *Cad Saúde Pública*. 2006;22:535-41.
- Galli M, Polo R, Saint-Marc, Walli R. Guidelines to describe morphologic and metabolic alterations (MMA) under ART: the Marrakech Classification. *Nutr Metab Disord HIV Infect*. 2002;1:25-9.
- Gervasoni C, Ridolfo AL, Trifiro G, Santambrogio S, Norbiato G, Musicco M, et al. Redistribution of body fat in HIV-infected women undergoing combined antiretroviral treatment. *Aids*. 1999;13:465-71.
- Goris AHC, Westterterp KR. Improved reporting of habitual food intake after confrontation with earlier results on food reporting. *Br J Nutr*. 2000;83:363-9.
- Hadigan C, Jeste S, Anderson EJ, Tsay R, Cyr H, Grinspoon S. Modifiable dietary habits and their relation to metabolic abnormalities in men and women with human immunodeficiency virus infection and fat redistribution. *Clin Infect Dis*. 2001;33:710-7.
- Hadigan C, Meigs JB, Corcoran C, Rietschel P, Piecuch S, Basgoz N, et al. Metabolic abnormalities and cardiovascular disease risk factors in adults with human immunodeficiency virus infection and lipodystrophy. *Clin Infect Dis*. 2001;32:130-9.

11. Hendricks KM, Dong KR, Tang AM, Ding B, Spiegelman D, Woods MN, et al. High-fiber diet in HIV-positive men is associated with lower risk of developing fat deposition. *Am J Clin Nutr.* 2003;78:790-5.
12. Kotler D, Rosenbaum K, Wang J, Pierson RN. Studies of body composition and fat distribution in HIV-infected and control subjects. *J Acquir Immune Defic Syndr Hum Retrovirol.* 1999;20:228-37.
13. Marins JRP, Jamal LF, Chen SY, Barros MBA, Hudes ES, Barbosa AA, et al. Dramatic improvement in survival among adult Brazilian AIDS patients. *Aids.* 2003;17:1675-82.
14. Martinez E, Mocroft A, Garcia-Viejo MA, Pérez-Cuevas JB, Blanco JL, Mallolas J, et al. Risk of lipodystrophy in HIV-1 infected patients treated with protease inhibitors: a prospective cohort study. *Lancet.* 2001;357:592-8.
15. National Heart, Lung, and Blood Institute; National Institutes of Diabetes and Digestive and Kidney Diseases. Clinical guidelines on the identification, evaluation and treatment of overweight and obesity in adults. Bethesda: National Institutes of Health; 1998. (NHI Publication 4083).
16. Shevitz A, Wanke C, Falutz J, Kotler D. Clinical perspectives on HIV-associated lipodystrophy syndrome: an update. *Aids.* 2001;15:1917-30.
17. Shevitz AH, Knox TA. Nutrition in the era of highly active antiretroviral therapy. *Clin Infect Dis.* 2001;32:1769-75.
18. Sichieri R, Everhart JE. Validity of a Brazilian food frequency questionnaire against dietary recalls and estimated energy intake. *Nutr Res.* 1998;18:1649-59.
19. Vella S. Future treatment perspectives. *J Acquir Immune Defic Syndr.* 2003;34(Suppl 1):95-100.
20. Willett W, Stampfer M. Implications of total energy intake for epidemiologic analyses. In: Willett W. *Nutritional epidemiology.* 2nd ed. New York: Oxford University Press; 1998. p. 273-301.
21. World Health Organization - WHO. Obesity: preventing and managing the global epidemic. Report. Geneva; 2000. [WHO Technical Report Series, 894]
22. World Health Organization - WHO. Diet, nutrition and the prevention of chronic diseases. Report. Geneva; 2003. [WHO Technical Report Series, 916]