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ORIGINAL RESEARCH

Anthropometric Risk Factors for Metabolic Syndrome in HIV patients

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OBJECTIVE: Metabolic syndrome, which affects the general population in epidemic proportions, is associated with a set of cardiovascular disease risk factors. The aims of this cross-sectional study were to determine the prevalence and investigate the risk factors associated with metabolic syndrome in outpatients living with HIV/AIDS using anthropometric and clinical evaluations.
METHOD: The study was carried out on 253 HIV infected outpatients. Metabolic syndrome was classified according to the National Cholesterol Education Program Adult Treatment Panel III (NCEP/ATPIII) and the International Diabetes Federation (IDF) criteria. Logistic regression was used to identify factors associated with the metabolic syndrome.
RESULTS: The prevalence of metabolic syndrome varied from 19.4% to 26.4%, according to the criterion used. The factors associated with it in the two classifications used, when adjusted by sex and BMI, were age (≥ 40years) and subscapular skinfold (> 12 mm). In the final model, using the NCEP/ATPIII criterion the risk factors associated with metabolic syndrome were age ≥ 40 years (OR = 3.18; CI95% = 1.42; 7.14) and subscapular skinfold > 12 mm (OR = 2.85, CI95% = 1.13; 7.17). In the final model, using the IDF criterion the risk factors associated with metabolic syndrome were age (OR = 3.38, CI95% = 1.61; 7.10) and subscapular skinfold > 12 mm (OR = 4.37, CI95% = 1.84; 10.39).
CONCLUSION: In clinical practice, the regular monitoring of subscapular skinfold can help in the identification of HIV infected individuals in risk of MS.

KEYWORDS: Metabolic Syndrome, HIV, Anthropometric.

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INTRODUCTION

The widespread use of antiretroviral therapy for the treatment of HIV has resulted in sustained reductions of morbidity and mortality associated with the infection.[1] However, long-term toxicity is becoming recognized, and a variety of metabolic abnormalities,[2,3] as well as the antiretroviral therapy itself have also been associated with metabolic complications that may increase patients' risk of cardiovascular disease.[4-6]

Metabolic syndrome (MS), which affects the general population in epidemic proportions, is associated with a set of cardiovascular disease risk factors.[7-9] HIV treatment guidelines recommend screening patients for metabolic complications and providing therapeutic interventions with the objective of preventing cardiovascular diseases.[10-11]

The aims of this cross-sectional study were to determine the prevalence and investigate risk factors associated with MS in outpatients living with HIV/AIDS using anthropometric and clinical evaluations.

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MATERIALS AND METHODS

Population and Study Design

This transversal study was performed on adult outpatients, in the Hospital Eduardo de Menezes-HEM, *Fundação Hospitalar do Estado de Minas Gerais-FHEMIG*, Belo Horizonte, Minas Gerais, Brazil. It was approved by the Ethical Review Board of the Universidade Federal de Minas Gerais (N. 0563.0.203.000-09).

The sample size (n = 1,400 inclusions) was calculated based on the total number of HIV-infected individuals who regularly attended the Infectious Diseases Service of the HEM/FHEMIG. The prevalence of metabolic syndrome in the population seen at our service ranged from 17% to 45.3%; the sample number was calculated on the basis of a prevalence of 50%, with a range of 6%, at a 95% confidence level. A minimum sample of 222 subjects was obtained. The study included HIV infected individuals who were over 18 and agreed to participate in the research through the signing of a Free and Informed Consent Agreement. Pregnant women with HIV were excluded. The subjects in this study were selected after drawing among those who were booked on the day for an appointment at the Hospital Eduardo de Menezes. All the selected subjects agreed to participate and had their data collected.

Data Collection

Data collection was performed by a single researcher, from July 2006 to August 2008. During the interviews, socio-economic, demographic and anthropometric information was obtained. Laboratory test results (CD4 cell count, viral load, serum lipids and blood glucose) performed on the date nearest the interview were collected from the medical records. All blood for tests were collected after exposure to a 12-hour fast.

Counting of T-CD4+ lymphocytes and viral load determination were performed by the Laboratory of the Fundação Ezequiel Dias, Belo Horizonte, Minas Gerais; other biochemical tests were processed the Clinical Analysis Laboratory of the HEM/FHEMIG. Counting of T-CD4+ lymphocytes was done by flow cytometry. The viral load was determined using the Versant® HIV 1 RNA 3.0 (bDNA) (Bayer®, Tarrytown, NY, USA) test, with a detection limit of 50 copies/ml of plasma. Plasma glucose, total cholesterol, HDL-cholesterol and triglycerides were analyzed enzymatically by colorimetric method (Vitros Chemistry Products, Johnson & Johnson Clinical Diagnostics®, Rochester, USA).

All procedures for obtaining anthropometric measurements were carried out in accordance with standardized criteria.[15]

The body circumferences were obtained using a tape to measure the patient in an upright position with the sole of the feet on the ground. The measurement of waist circumference was performed at the midpoint between the last rib and the iliac crest. In obese individuals, measurements were taken at the smaller diameter or true waist. The arm circumference was measured at the midpoint of the arm, located between the acromial process and the olecranon with the arm extended. The calf circumference was obtained at the largest circumference level of the calf, by sliding he tape upward till the largest circumference. [15]

Gauging skinfold was performed with the Cescorf® caliper (sensitivity of 0.1 mm, reading range 88 mm, pressure 10 g/mm^2), Three readings of each skinfold were obtained and the averge was considered. [15]

The subscapularis skinfold was measured obliquely to the longitudinal axis, following the direction of the ribs and located two centimeters below the lower angle of the scapula. In situations where the location was difficult to identify, such as in obese individuals, this was done with the arm bent back. The triceps skinfold thickness was measured at the back of the arm, parallel to the longitudinal axis, at half the distance between the upper-lateral edge of the acromion and the olecranon. The biceps skinfold thickness was measured along the longitudinal axis of the arm, on its anterior face at the point of greatest apparent circumference of the biceps. The suprailiac skinfold was measured obliquely along the longitudinal axis, at half the distance between the last rib and the iliac crest, on the medial axillary line. [15]

Definition of Metabolic Syndrome

MS was classified according to the criteria of the National Cholesterol Education Program Adult Treatment Panel III (NCEP/ATPIII) guidelines,[16] the International Diabetes Federation and the American Heart Association/ National Heart, Lung, and Blood Institute (IDF/AHA/ NHLBI).[17] The criteria were specifically modified by inserting the recorded diagnosis of diabetes in lieu of high levels of fasting serum glucose, and the recorded diagnosis of hypertension in lieu of high blood pressure.

The following cutoff points for central obesity of South American populations were used: (a) waist circumference > 102 cm for men or > 88 cm for women according to the NCET/ATPIII; (b) waist circumference ≥ 90 cm for men or ≥ 80 cm for women, according to the IDF.[18]

Statistical Analysis

Data analysis was carried out with Stata software, version 10.0, at a 5% significance level. Categorical variables were described through frequencies. The Shapiro Wilk test was used to evaluate the normality of continuous variables that were described by means, medians and dispersion measures (25 and 75 percentiles). The χ-Squared test or the Fischer's Exact test was used to compare frequencies. To compare means, the t-Student test was used. To compare medians, the U-Mann-Whitney test was used.

Table 1. Characteristics of HIV-infected outpatients, stratified by gender

Characteristic	Total n (%)	Men n (%)	Women n (%)	*p*
Age (years)				
< 40	105 (41,5)	73 (43.45)	32 (37,65)	
≥ 40	148 (58,5)	95 (56,55)	53 (62,35)	0.37
BMI (kg/m^2)				
< 18.5	18 (7.2)	10 (6.0)	8 (9.5)	
18.5 ≤ BMI < 25	153 (61.2)	110 (66.3)	43 (51.2)	
≥ 25	79 (31.6)	46 (27.7)	33 (39.3)	0.06
Illicit drug user				
No	241 (96.0)	156 (94.0)	85 (100.0)	
Yes	10 (4.0)	10 (6.0)	0 (0.0)	0.02
Alcoholic beverages user				
No	182 (71.9)	113 (67.3)	69 (81.2)	
Yes	71 (28.1)	55 (32.7)	16 (18.8)	0.02
Current tobacco smoker				
No	181 (74.1)	118 (70.2)	63 (74.1)	
Yes	72 (25.9)	50 (29.8)	22 (25.9)	0.52
Duration of HIV infection (years)				
< 6	124 (49.0)	83 (49.4)	41 (48.2)	
≥ 6	129 (51.0)	85 (50.6)	44 (51.8)	0.86
Viral load detectable				
No	154 (60.9)	102 (60.7)	52 (61.2)	
Yes	99 (39.1)	66 (39.3)	33 (38.8)	0.94
Current Antiretroviral therapy				
None	31 (12.4)	15 (9.0)	16 (19.2)	
Without PI	120 (48.2)	88 (53.0)	32 (38.6)	
With PI	98 (39.4)	63 (38.0)	35 (42.2)	0.03
Duration of antiretroviral therapy (years)				
< 5	100 (45.0)	73 (47.7)	27 (39.1)	
≥ 5	122 (55.0)	80 (52.3)	42 (60.9)	0.23

BMI, Body Mass Index; PI, Protease Inhibitor

Continuous variables with temporal information on infection diagnosis, antiretroviral therapy exposure and skinfold (triciptal, biciptal and subscapular) were categorized using the median as cutoff point. In terms of Body Mass Index, subjects were classified as underweight (BMI < 18.5 kg/m^2), normal weight (18.5 ≤ BMI < 25 kg/m^2) and overweight (BMI ≥ 25 kg/m^2).[15]

A logistic regression model was used to evaluate the association between metabolic syndrome and other investigated variables (demographic, socio-economic, clinical, anthropometric and laboratory).[19] The strength of the association was measured through Odds Ratio (OR), with 95% confidence interval (IC). The variables that presented $p < 0.25$ in univariate logistic regression analysis were selected for final model construction. Goodness-of-fit was verified with the Hosmer and Lemeshow statistic method. As initially noted, a p value < 0.05 was considered statistically significant.

RESULTS

Among the 253 HIV-infected individuals, the male gender corresponds to 66.4%. The mean age of the HIV-infected men and women was 41.2 ± 7.6 years (median: 40.4 years) and 41.9 ± 9.2 years (median: 41.6 years) ($p = 0.53$), respectively.

Illicit drug use and alcohol consumption was greater among men. The proportion of individuals not exposed to

Table 2. Metabolic syndrome and its defining criteria, by sex

Characteristic	Total n (%)	Men n (%)	Women n (%)	*p*
Metabolic syndrome (NCEP/ATPIII)				
No	183 (80.6)	132 (85.2)	51 (70.8)	
Yes	44 (19.4)	23 (14.8)	21 (29.2)	0.01
Metabolic syndrome (IDF/AHA/NHLBI)				
No	162 (73.6)	121 (80.1)	41 (59.4)	
Yes	58 (26.4)	30 (19.9)	28 (40.6)	0.002
Abdominal Obesity (NCEP/ATPIII)				
No	211 (84.4)	161 (97.0)	50 (59.5)	
Yes	39 (15.6)	5 (3.0)	34 (40.5)	< 0.0005
Abdominal Obesity (IDF/AHA/NHLBI)				
No	151 (60.4)	130 (78.3)	21 (25.0)	
Yes	99 (39.6)	36 (21.7)	63 (75.0)	< 0.0005
Hypertension				
No	231 (95.8)	155 (95.1)	76 (97.4)	
Yes	10 (4.2)	8 (4.9)	2 (2.6)	0.51
Diabetes				
No	153 (62.7)	101 (61.6)	52 (65.0)	
Yes	91 (37.3)	63 (38.4)	28 (35.0)	0.60
Low HDL (< 40 mg/dL (men) or < 50 mg/dL (women))				
No	65 (38.2)	50 (43.9)	15 (26.8)	
Yes	105 (61.8)	64 (56.1)	41 (73.2)	0.03
Triglycerides ≥ 150 mg/dL				
No	122 (50.4)	80 (49.1)	42 (53.2)	
Yes	120 (49.6)	83 (50.9)	37 (46.8)	0.55

NCEP/ATPIII, National Cholesterol Education Program Adult Treatment Panel III (NCEP/ATPIII); IDF/AHA/NHLBI, International Diabetes Federation and the American Heart Association/ National Heart, Lung, and Blood Institute; HDL, high-density lipoprotein

Table 3. Anthropometric characteristics of HIV-infected outpatients, stratified by gender

Anthropometry	n	Total Median(25-75%[a])	n	Men Median(25-75%)	n	Women Median(25-75%)	*p*
BMI (kg/m^2)	250	22.6 (20.5-25.7)	166	22.4 (20.4-25.3)	84	23.6 (21.4- 26.8)	0.04
Skinfold thickness (mm)							
Triciptal	252	7.0 (5.0-10.0)	167	6.0 (5.0-8.0)	85	11.0 (8.0-15.0)	0.0001
Biciptal	251	4.0 (3.0-6.0)	167	3.3 (3.0-5.0)	84	6.0 (4.3-9.3)	0.0001
Suprailiac	248	7.7 (5.0-12.0)	167	6.0 (4.0-9.0)	81	13.0 (8.0-15.0)	0.0001
Subscapular	245	12.0 (8.0-16.0)	165	10.0 (7.0-15.0)	80	15.0 (12.0-20.0)	0.0001
Body Circumferences (cm)							
Arm	251	28.0 ± 3.3[b]	167	28.5 ± 8.9	84	27.8 ± 3.9	0.10
Calf	251	34.6 ± 3.2	167	35.0 ± 2.9	84	33.8 ± 3.6	0.003
Waist	250	83.8 (78.5-89.5)	166	83.0 (78.5-89.0)	84	86.2 (79.8-94.0)	0.09

[a]Percentiles; BMI, Body Mass Index; b Means ± DV

Table 4. Odds ratio for characteristics associated with metabolic syndrome diagnosed according to NCEP/ATPIII and IDF/AHA/NHLBI criteria in HIV outpatients

Characteristic	Metabolic syndrome (NCEP/ATPIII)			Metabolic syndrome (IDF/AHA/NHLBI)		
	No	Yes	Odds Ratio (95%CI)	No	Yes	Odds Ratio (95%CI)
Gender						
Men	132	23	1	121	30	1
Women	51	21	2.36 (1.20; 4.64)	41	28	2.75 (1.47; 5.14)
Age (years)						
< 40	94	11	1	89	15	1
≥ 40	88	33	3.24 (1.54; 6.80)	73	43	3.49 (1.80; 6.79)
Alcoholic beverages user						
No	129	31	1	112	43	1
Yes	54	13	1.00 (0.49;2.06)	50	15	0.78 (0.40; 1.54)
Current tobacco smoker						
No	126	34	1	110	46	1
Yes	57	10	0.65 (0.30; 1.41)	52	12	0.55 (0.27; 1.13)
Duration of HIV infection (years)						
< 6	93	20	1	78	29	1
≥ 6	90	24	1.24 (0.64; 2.40)	84	29	0.93 (0.51; 1.69)
Viral load detectable						
No	112	29	1	95	39	1
Yes	71	15	0.82 (0.41; 1.63)	67	19	0.69 (0.37; 1.30)
Current Antiretroviral therapy						
None	17	8	1	17	8	1
Without PI	93	17	0.39 (0.06; 1,62)	79	26	0.70 (0.27; 1.81)
With PI	70	19	0.58 (0.21; 1.54)	64	24	0.80 (0.30; 2.09)
Duration of antiretroviral therapy (years)						
Without antiretroviral therapy	17	8	1	17	8	1
< 5	77	15	0.41 (0.15; 1.13)	62	23	0.79 (0.30; 2.07)
≥ 5	89	21	0.50 (0.19; 1.32)	83	27	0.69 (0.27; 1.78)
BMI (kg/m^2)			1.20 (1.09; 1.31)			1.21 (1.11; 1.32)
Triciptal Skinfold thickness						
≤ 7 mm	112	17	1	103	22	1
> 7 mm	70	27	2.54 (1.29; 5.00)	58	36	2.90 (1.56; 5.40)
Biciptal Skinfold						
≤ 4 mm	116	17	1	108	19	1
> 4 mm	66	27	2.79 (1.42; 5.50)	53	39	4.18 (2.20; 7.93)
Subscapular Skinfold						
≤ 12 mm	111	10	1	106	12	1
> 12 mm	68	32	5.22 (2.41; 11.30)	53	43	7.17 (3.49; 4.72)

NCEP/ATPIII, National Cholesterol Education Program Adult Treatment Panel III (NCEP/ATPIII); IDF/AHA/NHLBI, International Diabetes Federation and the American Heart Association/ National Heart, Lung, and Blood Institute; CI, Confidence Interval; BMI: Body Mass Index; PI, Protease Inhibitor

Table 5. Risk Factors for Metabolic Syndrome in HIV infected outpatients

Classification		Odds Ratio(95%CI)
Metabolic syndrome (NCEP/ATPIII)[a]		
	Age group ≥ 40	3.18 (1.42; 7.14)
	Subscapular Skinfold thickness > 12 mm	2.85 (1.13; 7.17)
Metabolic syndrome (IDF/AHA/NHLBI)[b]		
	Age group ≥ 40	3.38 (1.61; 7.10)
	Subscapular Skinfold thickness > 12 mm	4.37 (1.84; 10.39)

[a,b] Ajusted by sex and body mass index CI, Confidence Interval; NCEP/ATPIII, National Cholesterol Education Program Adult Treatment Panel III; (NCEP/ATPIII); IDF/AHA/NHLBI, International Diabetes Federation and the American Heart Association/National Heart, Lung, and Blood Institute.

antiretrovirals was greater among women, as shown in Table 1.

The overall prevalence of MS, according to the IDF/AHA/NHLBI and the NCEP/ATPIII criteria, was 26.4% and 19.4%, respectively. Independently of the criterion used, the prevalence of metabolic syndrome, low HDL and abdominal obesity was greater among women.

According to the IDF/AHA/NHLBI criterion, the prevalence of MS in the age group < 40 years, was 14.4% (15/104); in the age group ≥ 40 years it was 37.1% (43/116); this difference is statistically significant (p <0.005). According to the NCEP/ATPIII criterion, the respective prevalences were lower, at 10.4% (11/106) in the < 40 age group and 27.3% (33/121) in ≥ 40 age group. This difference is also significant (p = 0.001).

The men had lower BMI and skinfold measurements than women. Men also showed greater calf circumference values than women, as shown in Table 3.

Table 4 shows the results of univariate logistic regression analysis of risk factors for MS. This analysis of univariate logistic regression allowed the selection and use of different variables according to the diagnostic criteria used, and the variables: age, sex, BMI, all skinfold, calf circumference and exposure to antiretroviral therapy used for the SM NCEP/ATPIII and the variables: age, sex, BMI, all skinfold, calf circumference and smoking when used the IDF/AHA/NHLBI.

In the final model using the NCEP/ATPIII criterion, adjusted by BMI and sex, the risk factors associated with MS in HIV infected individuals were age ≥ 40 (OR = 3.18; CI95% = 1.42; 7.14) and subscapular skinfold > 12 mm (OR = 2.85, CI95% = 1.13; 7.17). In the final model using IDF/AHA/NHLBI criterion, adjusted by BMI and sex, the risk factors associated with MS in HIV infected individuals were also age > 40 (OR = 3.38, CI95% = 1.61; 7.10) and subscapular skinfold > 12 mm (OR = 4.37, CI95% = 1.84; 10.39), table 5.

DISCUSSION

In this study we note that the prevalence of MS in HIV infected outpatients varied from 19.4% to 26.4%, according to the criterion used. The factors associated with MS, when adjusted by sex and BMI, were similar in the two classifications used. For individuals infected with HIV or Aids, the variables of age (≥ 40) and subscapular skinfold (> 12 mm) were associated with MS.

Previous studies on the prevalence of MS in HIV infected individuals, carried out in Brazil, found prevalence levels that varied between 15% and 36%.[20-23] Studies performed in Brazil on non HIV infected individuals found a prevalence of MS varying from 25.4% to 30%.[24-26] Differences between the studied population groups and diagnostic criteria make it difficult to compare these reports.

In this study, the prevalence of MS, independent of the criterion used was greater among women infected with HIV. This result was also found by other investigations.[5,13,20,22]

The main limitation of this study relates to the distribution of MS defining criteria that may have been underestimated through the use of secondary data. The absence of information in medical records impeded the classification of individuals that had two defining conditions for metabolic syndrome and who did not have information on seric levels of HDL or triglycerides. This could have contributed to underestimating the prevalence of MS in the population studied. This limitation has also been noted in other studies that used secondary data in the investigation of MS in HIV infected patients.[13,14,27] The fact of not having used alternative criteria for fasting glycemia, blood pressure and serum triglycerides, such as the use of antihypertensive, antidiabetic or lipid lowering drugs may also have contributed towards underestimating the distribution MS defining conditions and, consequently, its prevalence.

Other limitations that merit consideration are related to the epidemiological design. The main limitations of a cross-sectional study in identifying risk factors is the temporal bias, because the time sequence cannot be established and because of the survival bias, both of which may affect prevalence.

Regardless of the criterion used to classify MS, the ≥ 40 age group was identified as a risk factor for this syndrome. Studies had already identified age[22,28-31] and the ≥ 40 age group[20] as independent risk factors for MS in

individuals infected with HIV. Individuals in the ≥ 40 age group who participated in this study presented a greater prevalence of obesity, diabetes and hypertension when compared with younger groups (data not shown).

In this study, a subscapular skinfold thickness > 12 mm was identified as a risk factor for MS, regardless of the criterion used. Since the two models for MS were adjusted by BMI and sex, this result cannot be attributed to the increase in body weight nor to the fact that women presented greater skinfold values when compared to the men. These results indicate that the accumulation of fat in the trunk region is an important risk factor; moreover, they are corroborated by studies, carried out by Jacobson et al.,[32] which noted that the increase in the trunk fat/body fat ratio was associated with metabolic syndrome, after being adjusted for BMI and weight gain. The accumulation of fat in the trunk region has been noted in individuals infected with HIV, in the absence of clinical lipodystrophy.[33]

In conclusion, Metabolic syndrome was associated with the ≥ 40 age group and with increase in subscapular skinfold thickness. In clinical practice, regular monitoring of subscapular skinfold thickness can help in the identification of HIV infected individuals at risk of MS.

AUTHOR PARTICIPATION

Leal JA: conception, design, acquisition of data, intellectual and scientific content of the study, writing of the manuscript, critical revision and final approval of the manuscript; Fausto MA conception, design, intellectual and scientific content of the study, manuscript writing and critical review; Carneiro M: design, intellectual and scientific content of the study, writing of the manuscript.

CONFLICT OF INTEREST

Authors declare no conflict of interest regarding this project.

FATORES DE RISCO ANTROPOMÉTRICOS PARA SÍNDROME METABÓLICA EM PACIENTES COM HIV

OBJETIVO: A síndrome metabólica afeta a população em geral em proporções epidêmicas e está associada a um conjunto de fatores de risco de doenças cardiovasculares. Os objetivos deste estudo transversal foram determinar a prevalência e investigar os fatores de risco associados à síndrome metabólica em pacientes ambulatoriais afetados por HIV/AIDS usando avaliações antropométricas e clínicas.

MÉTODO: O estudo foi realizado em 253 pacientes ambulatoriais infectados pelo HIV. A síndrome metabólica foi classificada de acordo com o National Cholesterol Education Program Adult Treatment Panel III (NCEP/ATPIII) e os critérios da International Diabetes Federation (IDF). A regressão logística foi utilizada para identificar os fatores associados à síndrome metabólica.

RESULTADOS: A prevalência de síndrome metabólica variou entre 19,4% e 26,4%, de acordo com o critério utilizado. Os fatores associados nas duas classificações utilizadas, quando ajustados por sexo e IMC, foram: idade (≥ 40 anos) e subescapular (> 12 mm). No modelo final, utilizando o critério do NCEP/ATPIII os fatores de risco associados à síndrome metabólica foram idade ≥ 40 anos (OR = 3,18; IC95% = 1,42; 7,14) e dobra cutânea subescapular > 12 mm (OR = 2,85, IC95% = 1,13; 7,17). No modelo final, utilizando o critério IDF os fatores de risco associados à síndrome metabólica foram idade (OR = 3,38, IC95% = 1,61; 7,10) e dobra cutânea subescapular > 12 mm (OR = 4,37, IC95% = 1,84; 10,39).

CONCLUSÃO: Na prática clínica, o acompanhamento regular da dobra cutânea subescapular pode ajudar na identificação de indivíduos infectados pelo HIV em risco de MS.

PALAVRAS-CHAVE: síndrome metabólica, HIV, Antropometria

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