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Nutritional status and CD4 cell counts in patients with HIV/AIDS receiving antiretroviral therapy

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ABSTRACT

Introduction: Even with current highly active antiretroviral therapy, individuals with AIDS continue to exhibit important nutritional deficits and reduced levels of albumin and hemoglobin, which may be directly related to their cluster of differentiation 4 (CD4) cell counts. The aim of this study was to characterize the nutritional status of individuals with human immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS) and relate the findings to the albumin level, hemoglobin level and CD4 cell count. **Methods:** Patients over 20 years of age with AIDS who were hospitalized in a university hospital and were receiving antiretroviral therapy were studied with regard to clinical, anthropometric, biochemical and sociodemographic characteristics. Body mass index, percentage of weight loss, arm circumference, triceps skinfold and arm muscle circumference were analyzed. Data on albumin, hemoglobin, hematocrit and CD4 cell count were obtained from patient charts. Statistical analysis was performed using Fisher's exact test, Student's t-test for independent variables and the Mann-Whitney U-test. The level of significance was set to 0.05 ($\alpha = 5\%$). Statistical analysis was performed using Statistical Package for the Social Sciences (SPSS) 17.0 software for Windows. **Results:** Of the 50 patients evaluated, 70% were male. The prevalence of malnutrition was higher when the definition was based on arm circumference and triceps skinfold measurement. The concentrations of all biochemical variables were significantly lower among patients with a body mass index of less than 18.5kg/m². The CD4 cell count, albumin, hemoglobin and hematocrit anthropometric measures were directly related to each other. **Conclusions**: These findings underscore the importance of nutritional follow-up for underweight patients with AIDS, as nutritional status proved to be related to important biochemical alterations.

Keywords: HIV/AIDS. Nutritional status. Anemia

INTRODUCTION

With the introduction of highly active antiretroviral therapy (HAART), the population infected with human immunodeficiency virus (HIV) has experienced a substantial increase in life expectancy and quality of life. However, malnutrition remains a concern in patients with acquired immune deficiency syndrome (AIDS)[1]. Individuals with HIV undergo various physiological alterations beginning in the early phase of the infection. Malnutrition was one of the first complications of AIDS to be recognized and one of the most frequent diagnoses in the population infected with HIV. Several studies have demonstrated an association between lean mass depletion/malnutrition and disease progression/patient survival[2,3]. The impaired nutritional status of patients with HIV is partially caused by the reduction in calorie intake, the occurrence of opportunistic diseases and the hypercatabolic action of the body in an attempt to control viral replication and recompose the immune system[4]. In a cross-sectional study using secondary information from the Brazilian Mortality Information System (*Sistema de Informações sobre Mortalidade* - SIM), 7.4% of cases of death were associated with endocrine, nutritional and metabolic diseases[5].

In patients with HIV, there is an association among low albumin levels[6,7], low body mass index (BMI) and CD4 count < 200 cells/mm³. These variables are indications of nutritional deficiency, which is also demonstrated by the high prevalence of anemia, the etiological factors of which include the side effects of medications, opportunistic diseases and HIV itself[8,9]. The risk of developing AIDS-associated anemia is increased in patients with a CD4 cell count < 200 cells/mm³, those taking zidovudine, those with a history of fever, those with oral candidiasis or bacterial pneumonia, those of African descent, those of female sex, those with lower muscle mass, those of advanced age or those with a high viral load[10,11].

Years after the introduction of HAART in Brazil, groups of patients with HIV still exhibit clinical and nutritional characteristics common to the pre-HAART era. Thus, the aim of the present study was to identify the nutritional profile of this population and determine how this profile relates to important biochemical variables.

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METHODS

Patients hospitalized in the Infectious Disease Clinics of the Oswaldo Cruz University Hospital in the City of Recife in Pernambuco (Brazil) between March and October 2011 were evaluated. This institution is a reference hospital for infectious diseases in the State of Pernambuco (northeastern Brazil) and primarily treats a population with a low socioeconomic status in addition to homeless individuals and drug users. The following were the inclusion criteria: age between 20 and 60 years or older, diagnosis of HIV, treatment with HAART and agreement to participate in the study through a signed statement of informed consent. Patients who required intensive care during hospitalization were excluded, and patients using ferrous sulfate, those with bleeding or those who had undergone surgery in the last six months were also excluded.

Data on albumin, hemoglobin, hematocrit and CD4 cell count were obtained from patient charts. The following were the reference values for findings considered normal: albumin higher than 3.5g/dl in both sexes; hemoglobin equal to or higher than 14g/dl and hematocrit equal to or higher than 44% for men; and hemoglobin equal to or higher than 12g/dl and hematocrit equal to or higher than 38% for women. For stratification of anemia, a hemoglobin concentration lower than 8g/dl was considered severely reduced, a hemoglobin concentration between 8 and 12g/dl was considered moderately reduced and a hemoglobin concentration equal to or higher than 12g/dl was considered mildly reduced or normal. The CD4 cell count was interpreted based on the recommendations of the Brazilian Ministry of Health, which uses 200 cells/mm³ as the cutoff point (lower than 200cells/mm³ is one of the criteria used to define AIDS in patients with HIV, together with nutritional status and the presence of opportunistic diseases)[12].

The nutritional evaluation was performed once within 72h of admission and included an anthropometric evaluation and history of weight loss. Weight was determined using a digital scale with a maximal capacity of 140kg and a precision of 100g. Height was determined using a metal stadiometer coupled to the digital scale with a capacity of 2m and a precision of 1cm. Arm circumference (AC) and triceps skinfold (TSF) were measured following the methods described by Lohman et al[13]. For bed-ridden patients, weight and height were estimated using formulas proposed by Chumlea et al[14]. Calf circumference, AC, TSF and subscapular skinfold were measured following the methods described by Lee and Nieman[15], and the height of the knee was measured following the method described by Chumlea et al[14]. Arm muscle circumference (AMC) was estimated using the formula proposed by Frisancho[16].

Based on the BMI, the patients were classified as either underweight (BMI < 18.5kg/m²) or adequate weight (BMI ≥ 18.5kg/m²). The percent weight loss was stratified as < 10% or ≥ 10% in relation to habitual weight. AC, TSF and AMC measurements were compared to the references values proposed by Blackburn and Thornton[17], and classified as < 90% or ≥ 90% adequate.

The variables were represented by pertinent descriptive statistics: absolute (n) and relative (%) frequency or mean and standard deviation (SD). Fisher's exact test was used to determine associations among the categorical variables. Student's t-test for independent variables was used to compare means among groups of interest. The Mann Whitney U-test was used to analyze the difference between the medians of two data sets. The level of significance was set to 0.05 (α = 5%). The statistical analysis was performed using SPSS 17.0 software for Windows.

Ethical considerations

This study received approval from the local Human Research Ethics Committee under process number 014/2011.

RESULTS

Fifty patients were evaluated (mean age: 36.54 ± 12.1 years). **Table 1** displays the characteristics of the sample.

The mean BMI was 19.64kg/m² (SD 4.6kg/m²). The prevalence of malnutrition differed based on the measure employed. AC and TSF adequacy were associated with a higher number of diagnoses of malnutrition. Among the patients

TABLE 1 - Demographic, nutritional and clinical characteristics of patients with HIV receiving HAART and hospitalized at the Oswaldo Cruz University Hospital in Recife, Brazil, in 2011.

Characteristic	Number	Percentage
Demographic		
male sex	35	70.0
age: 19-39 years	33	66.0
age: 40-59 year	14	28.0
age ≥ 60 years	6	6.0
Nutritional		
BMI < 18.5kg/m²	26	52.0
weight loss ≥ 10%	35	70.0
AMC < 90% adequate	30	60.0
TSF < 90% adequate	41	82.0
AC < 90% adequate	41	82.0
Clinical		
time since diagnosis ≥ 2 years	28	56.0
CD4 cell count < 200 cells/mm³	36	70.0
concentration of albumin < 3.5g/dl	36	70.0
hemoglobin < 12g/dl	40	80.0
hematocrit < 38%	41	82.0

HIV: human immunodeficiency virus; HAART: highly active antiretroviral therapy; BMI: body mass index; AMC: arm muscle circumference; TSF: triceps skinfold; AC: arm circumference; CD4: cluster of differentiation 4.

considered malnourished based on the BMI, all (100%) had a weight loss higher than 10% of the habitual weight.

When classified based on the BMI, both groups of patients had different means with regard to the number of leukocytes and lymphocytes, the hematocrit and the levels of hemoglobin and serum albumin, with statistically significant differences in the last three measures **(Table 2**).

The mean albumin level was 3.06g/dl (SD 0.69g/dl). Diminished serum albumin levels were associated with lower CD4 cell counts and weight loss greater than 10% in relation to habitual weight (p = 0.00 and 0.01, respectively). BMI, AC, TSF, and time since diagnosis were not significantly associated with serum albumin level.

Statistically significant differences in the CD4 cell count were found in relation to weight loss, serum albumin level, and BMI. The CD4 cell count was not significantly associated with AC, TSF or time since diagnosis **(Table 3**).

In the overall sample, 84% were classified as anemic (86% of women and 74.28% of men), with no statistically significant sex

TABLE 2 - Biochemical parameters according to BMI in patients with HIV receiving HAART and hospitalized at the Oswaldo Cruz University Hospital in Recife in Brazil, 2011.

	Malnourished (N=26)		Eutrophic (N=24)		
	M	SD	M	SD	p-value
Leukocytes (cells/mm³)	5.296	2.999	5.674	3.408	0.68
Lymphocytes (cells/mm³)	926.38	737.45	1313.12	794.30	0.08
Hemoglobin (g/dl)	9.57	1.81	11.11	2.46	0.01
Hematocrit (%)	28.66	5.02	32.92	7.19	0.02
Albumin (g/dl)	2.81	0.71	3.353	0.56	< 0.01

BMI: body mass index; HIV: human immunodeficiency virus; HAART: highly active antiretroviral therapy. Student's t-test. M: mean; SD: standard deviation.

TABLE 3 - Association among CD4 cell count, albumin level and nutritional measures in patients with HIV receiving HAART and hospitalized at the Oswaldo Cruz University Hospital in Recife, Brazil, in 2011.

	< 200 cells/mm³		≥ 200 cells/mm³		Total		Mann-Whitney	
	n 36	% 72	n 14	% 28	n 50	% 100.0	U test	p-value
WL < 10%	6	12.0	10	20.0	16	32.0		
WL ≥ 10%	30	60.0	4	8.0	34	68.0		
M±SD	23.03 ± 13.08		8.3 ± 6.67				83,000	0.00
Alb < 3.5g/dl	31	62.0	5	18.0	36	80.0		
Alb ≥ 3.5g/dl	5	10.0	9	10.0	14	20.0		
M±SD	2.87 ± 0.5		3.57 ± 0.39				102,500	0.00
AMC < 90% adeq	27	54.0	4	8.0	31	62.0		
AMC ≥ 90% adeq	9	18.0	10	20.0	19	38.0		
M±SD	87.96 ± 14.95		99.63 ± 14.33				136,000	0.00
BMI < 18.5kg/m²	23	46.0	3	6.0	26	52.0		
BMI ≥ 18.5kg/m²	13	26.0	11	22.0	24	48.0		
M±SD	18.36 ± 2.6		22.93 ± 3.56				110,500	0.02
Hem < 12mg/dl	32	64.0	8	16.0	40	80.0		
Hem ≥ 12mg/dl	4	8.0	6	12.0	10	40.0		
M±SD	9.76 ± 1.67		11.73 ± 1.73				135,000	0.01

CD4: cluster of differentiation 4; HIV: human immunodeficiency virus; HAART: highly active antiretroviral therapy. Mann-Whitney U test; WL: weight loss; M: mean; SD: standard deviation; Alb: albumin; AMC: arm muscle circumference; BMI: body mass index; Hem: hemoglobin.

TABLE 4 - Associations among the degree of anemia, BMI, weight loss, albumin level, CD4 cell count and leukocyte count in patients with HIV receiving HAART hospitalized at the Oswaldo Cruz University Hospital in Recife, Brazil, in 2011.

	Severe		Moderate		Mild/normal		Total		
	n	%	n	%	n	%	n	%	p-value
	9	18.0	31	62.0	10	20.0	50	100.0	
CD4 < 200 cells/mm³	9	18.0	22	44.0	4	8.0	35	70.0	0.01
CD4 ≥ 200 cells/mm³	0	0.0	9	18.0	6	12.0	15	30.0	
Alb < 3.5g/dl	9	18.0	23	46.0	4	8.0	36	72.0	
Alb ≥ 3.5g/dl	0	0.0	8	16.0	6	12.0	14	28.0	0.01
BMI < 18.5kg/m²	6	12.0	19	38.0	1	2.0	26	52.0	
BMI ≥ 18.5kg/m²	3	6.0	12	24.0	9	18.0	24	48.0	0.01
WL < 10%	0	0.0	7	14.0	8	16.0	15	30.0	
WL ≥ 10%	9	18.0	24	48.0	2	4.0	35	70.0	0.00
Leuko < 5,000,000	7	14.0	20	40.0	2	4.0	29	58.0	
Leuko 5-10,000,000	2	4.0	9	18.0	5	10.0	16	32.0	
Leuko > 10,000,000	0	0.0	2	4.0	3	6.0	5	10.0	0.04

BMI: body mass index CD4: cluster of differentiation 4; HIV: human immunodeficiency virus; HAART: highly active antiretroviral therapy; Alb: albumin; WL: weight loss; Leuko: leukocytes. Pearson's chi-squared test and Fisher's exact test.

difference. Regarding the degree of severity, 62% had moderate anemia and 18% had severe anemia with no statistically significant sex difference. The degree of anemia was associated with CD4 cell count, albumin level, BMI, weight loss and leukopenia **(Table 4)**.

DISCUSSION

The Joint United Nations Program on HIV/AIDS (UNAIDS) reports the feminization of HIV, and in sub-Saharan Africa, six in 10 adults living with HIV are currently woman[18]. However, this characteristic was not supported by the findings of the present study, which may be explained by the advanced degree of infection in the patients analyzed, as women are generally more concerned with their health and consequently more likely to adhere to HAART. Moreover, with the introduction of erectile dysfunction medications and the aging of the population worldwide, there has been an increase in the incidence of AIDS among elderly individuals. However, the present sample was composed mainly of young, sexually active, promiscuous individuals.

The findings revealed a malnourished sample with important clinical and biochemical alterations. Despite the introduction of highly active antiretroviral therapy, these characteristics have also been reported by other studies[2,3,19]. The mean BMI in the present investigation differed from that reported by Silva et al.[20] in 2010, who found a mean BMI of 24.4kg/m² (SD 4.3kg/m²) in patients receiving HAART in the City of Sao Paulo (Brazil), and that reported by Kroll et al.[21], who found that the prevalence of excess weight (overweight or obesity) was higher than the prevalence of malnutrition among HIV/AIDS patients[21]. This difference may be explained by the patient profile, as the subjects in the studies cited were in outpatient follow-up, whereas those in the present study were hospitalized and therefore in worse clinical condition.

Based on the BMI, 52% of the patients were diagnosed with malnutrition. However, the AMC, AC and TSF measures proved to be even more sensitive (60, 82 and 82%, respectively). Ribeiro[22] reported similar results, as 41% of the population analyzed had a BMI < 18.5kg/m². In a study conducted in the City of Porto Alegre (State of Rio Grande do Sul, Brazil) in 2009, the prevalence of malnutrition among patients using of HAART was only 6.4% among men and 12.7% among women[23]. It should be noted that while the population in the study cited used antiretroviral therapy, one of the inclusion criteria was being asymptomatic, which differed from the inclusion criteria of the present study. A study involving hospitalized patients with HIV found results similar to those in the present study regarding malnutrition based on AC and AMC measurements, with percentages of 81 and 84%, respectively, but only 5% based on the TSF, demonstrating that the population analyzed exhibited lean mass depletion but not fat mass depletion[24]. In contrast, the present sample exhibited both lean mass and fat mass depletion.

Oliveira[24] previously reported a mean serum albumin level of 3.18g/dl (SD 0.91g/dl), which is similar to the value reported herein. Indeed, only 35% of the sample in the present investigation had serum albumin levels within the range of normality. As a negative acute-phase protein, albumin is a difficult malnutrition indicator to evaluate.

In 1995, Luder et al.[25] found that values for anthropometric parameters and CD4 lymphocyte counts were notably lower in patients who had experienced weight loss. The present study confirms this finding, as statistically significant differences were found in some of the anthropometric measures evaluated, in the CD4 cell count and in the serum albumin level between patients with a weight loss ≥ 10% of their habitual weight and those with a weight loss less than 10% of their habitual weight. Moreover, associations were found among low albumin levels, below-normal BMI and CD4 cell count < 200 cells/mm³ in patients infected with HIV, which is in agreement with findings reported in previous studies[6,7]. These associations are explained by the association of a low CD4 cell count with more advanced stages of infection, implying a higher frequency of opportunistic infections, which affect nutritional status by increasing metabolism and diminishing food intake because of factors such as fever, oral and esophageal lesions, anorexia and diarrhea. A reduced BMI and hypoalbuminemia reflect a reduction in nutritional status characterized by a protein-energy malnutrition.

The prevalence of anemia in patients with AIDS is estimated to be between 63 and 95%[26]. Thus, the rate of 84% in the present study is in agreement with findings reported in the literature. This high rate of anemia has multiple causes, such as bone marrow dysfunction caused by the virus, formation of anti-erythrocyte and anti-leukocyte antibodies and certain medications. The reduction in hemoglobin concentration is also caused by the shortage of micronutrients related to hematopoiesis, which is characteristic of severe nutritional deficiencies[26]. Patients with AIDS and the acute phase response are nutritionally compromised and have anemia that does not seem to depend on the recent intake of iron.[27] Correction of nutritional deficiencies includes the correction of iron deficiency and vitamin B12 and B9 deficiencies that lead to anemia[28].

Despite the advances achieved with HAART, studies have demonstrated a high incidence of anemia in patients submitted to this form of therapy that seems to be associated with the hematologic toxicity of antiretroviral agents, which can inhibit the formation of progenitor blood cells[29]. Berhane et al.[30] reported that the use of HAART for six months is sufficient for the development of anemia, which may become aggravated depending on the duration of the use of the drugs. Moyle et al.[31] reported that patients receiving HAART for 48 weeks may develop anemia and associated this finding with the possible suppression of bone marrow activity induced by the treatment. Other risk factors for anemia in patients with HIV are CD4 cell count < 200 cells/mm³, female sex, advanced age, low BMI, African descent and a history of fever and oral candidiasis[32]. In the present sample, anemia severity was associated with a low CD4 cell count, albumin level less than 3.5g/dl, BMI less than 18.5kg/m², weight loss higher than 10% of the habitual weight and leukopenia. These results are associated with the worsening of side effects because of food insecurity that leads to the deterioration of patients' nutritional condition and decreases adherence to the treatment, leading to further progression of the disease, increased resistance to antiretroviral therapy and increased costs of medical care for these patients[33].

The limitations of this study are related to the lack of consideration of the time of diagnosis or patient adherence to antiretroviral therapy. At the time of data collection, all patients were receiving HAART while hospitalized. Furthermore, because this was a cross-sectional study, we are limited to describing the occurrence of clinical and nutritional characteristics of patients living with HIV/AIDS who were treated at the Hospital Oswaldo Cruz.

In the present study, the population with HIV exhibited worrisome characteristics from a clinical and nutritional standpoint. The high prevalence of malnutrition defined based on all anthropometric measures was associated with anemia, low albumin levels and low CD4 cell counts. These findings underscore the importance of the nutritional evaluation and follow up of hospitalized patients with HIV receiving HAART, as nutritional status is related to other parameters, which, when considered together, affect the condition and quality of life of such individuals.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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