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Factors associated with neurocognitive disorders in people living with HIV aged ≥ 50 years old in Brazil: a cross-sectional study

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ABSTRACT

Introduction: There is a high prevalence of HIV-associated neurocognitive disorders (HAND), especially in people living with HIV (PLWH) who are ≥50 years old. **Objective:** The objective of this study was to identify the factors associated with HAND in PLWH who are ≥50 years old. **Methods:** This is a cross-sectional study involving 48 patients (Mean=59.6 years). We collected sociodemographic, clinical, and anthropometric data, and the instrumental activities of daily living (IADL) and International HIV Dementia Scale (IHDS) were administered for neurocognitive evaluation. **Results:** A total of 75% of individuals had HANDs, including 88.89% with asymptomatic disorders and 11.11% with mild/moderate disorders. IHDS scores were positively correlated with educational level, nutritional status, and viral load (VL) at the time of diagnosis, while negatively correlated with the number of diseases, number of medications, and blood glucose levels. **Conclusion:** To the best of our knowledge, this is one of few studies conducted exclusively with elderly PLWH that investigated the factors associated with HAND in an inland city from a developing country, showing that the main predictors of HANDs were education, VL at diagnosis, and blood glucose. Hence, results could support future studies and interventions among PLWH elsewhere, where resources are limited and HIV assistance may be more precarious and difficult.

Keywords: aging; antiretroviral therapy, highly active; neurocognitive disorders; HIV; Acquired Immunodeficiency Syndrome; communicable diseases.

INTRODUCTION

Between 2010 and 2020, the incidence of HIV decreased by 30% worldwide, and the mortality rate of acquired immune deficiency syndrome (AIDS) decreased by 42%; during the same period, there was a 21% in the number of new HIV cases in Latin America, and more than 342,000 cases of HIV have been reported in Brazil since 2007. Even with the results of antiretroviral therapy (ART), the role of HIV in the development of chronic diseases is evident. In addition, HIV treatment itself can potentiate the development of cardiovascular and metabolic problems due to the adverse effects of exposure to therapy[1].

HIV is a causal factor of several comorbidities due to the inflammatory condition and direct degenerative potential. The central nervous system (CNS) is one of the tissues that suffers from these effects, with evident neurodegeneration sustained by HIV toxicity; this toxicity can reproduce in the brain parenchyma, especially in glial cells, thereby releasing neurotoxic proteins, causing inflammation in nervous tissues, and contributing to neurocognitive impairment in PWLH[2].

The amount of virus isolated in the CNS, the presence of irreversible lesions before ARV administration, or even the inflammatory state generated by immune activation are possible explanations for the emergence of HIV-associated neurocognitive disorders (HANDs)[3]. HANDs are a relevant public health problem, as they are present in approximately 30% to 70% of PLWH and are more prevalent in PLWH aged 50 years or older[4,5]. Although few studies have been conducted exclusively with PLHIV aged ≥50 years, the evidence reinforces the associations between older age, lower education, and low levels of CD4+ T cells and HAND, as well as the cognitive impairment present even when viral load (VL) is undetectable[6].

Recently, there has been a reduction in cases of HIV-associated dementia (HAD) and a higher frequency of milder disorders, such as mild neurocognitive disorder (MND) and asymptomatic neurocognitive impairment (ANI)[7]. HANDs hinder adherence to ARVs, leading to important health risks that can cause negative clinical outcomes among patients and worsening diseases. Therefore, early detection is essential for improving prognosis, promoting health status, strengthening immunity, and avoiding premature neurodegeneration[8]. HAND screening is also important since studies indicate that neurocognitive disorders are more prevalent in PLWH when compared to the general population and may be linked to higher risks of mortality[9-10].

Despite the advancements in treating HIV, the role of infection in developing neurocognitive disorders deserves attention. The current study aims to identify the factors associated with HANDs in PLWH aged ≥50 years living in Francisco Beltrão, Paraná, Brazil. To the best of our knowledge, this is one of the few investigations conducted entirely with PLWH ≥50 years that explored these factors in an inland city from a developing country.

METHODS

The current cross-sectional study included patients who were being followed up at a Specialized Care Service (SAE) in Francisco Beltrão, Paraná, Brazil. The inclusion criteria were males and females ≥50 years old, positive serology for HIV, residing in Francisco Beltrão, monitored by the SAE, and who agreed to participate. The exclusion criteria were as follows: death; lost to follow-up; diagnosed with severe neoplasms; neuropsychiatric diseases that prevented participation in data collection; patients who did not walk; and those who did not complete the questionnaires.

Procedures

A trained multidisciplinary team individually assessed participants. Participation was voluntary, and confidentiality was ensured. Those who agreed to participate signed consent forms. The research ethics committee also approved of this study.

Patients were evaluated in the morning, using different procedures and instruments[11-19]. First, while fasting for at least three hours and with an empty bladder, using minimal clothing, barefoot, standing, and static, an anthropometric assessment took place, along with bioimpedance procedures. Next, a sociodemographic questionnaire, along with the Portuguese versions of the following tests were used: the International HIV Dementia Scale (IHDS), the Daily Life Activities Scale (IADL), the polypharmacy assessment, the mini-nutritional assessment (MNA), the 15-item geriatric depression scale (GDS), gait speed (GS), evaluation of sarcopenia and frailty syndrome, and the International Physical Activity Questionnaire (IPAQ) short version. Additional clinical data, such as the date of HIV diagnosis, time of infection, and results of laboratory tests, were obtained from medical records.

Dependent variable

Neurocognitive functioning was evaluated using the IHDS, which assesses memory, motor speed, and psychomotor functioning and can be easily applied by any professional, which is especially useful in places with limited resources[8,13]. In this study, the original cutoff point (<10) for the IHDS was selected because it was the most useful and ideal for screening for HANDs[8] and because this value is the most commonly used cutoff in international studies, thus facilitating the comparison of results. The instrument has been validated in Brazil[13].

Independent variables

The Lawton scale, which evaluates the IADL, has nine domains scored from one to three. Independence is represented by a score of 27, partial dependence is represented by a score between 18 and 26, and total dependence is represented by a score of 17 points or less[9]. Polypharmacy was defined as the use of five or more drugs, counted by the number of active ingredients, excluding ARV[10]. Adherence to ARV was assessed through three questions. When any of the answers was "yes", it was considered that the patient did not have adherence to ARV; only when all answers were "no" was adherence to ARV[11].

Nutritional status was assessed with the aid of the MNA[12]. Normality is represented by a score between 24 and 30 points; nutritional risk is represented by a score between 17 and 23.5, and malnutrition is represented by a score below 17[14]. BMI was calculated using the ratio between the weight in kilograms and the square of the height in meters, appropriate according to the characteristics of elderly individuals.

Screening for depression was performed using the GDS, which is a 15-item scale. Scores above 5 indicate a risk of depression[15]. In turn, gait speed (GS) was assessed by asking the patient to walk at 4.57 meters, marked on the ground, at their usual speed and without assistance. Orthoses were maintained during the test. GS is part of the criteria for frailty and sarcopenia, and in frailty syndrome, the change varies according to height and sex, and the cutoff point is in seconds[16]. The evaluation of frailty syndrome uses five criteria, and each criterion is worth one point: hand grip strength (HGS), GS, weight loss, exhaustion, and low physical activity. Frailty was determined based on grip strength, gait speed, unintentional weight loss, exhaustion, and low physical activity. These tasks are scored on a scale of 0 to 1. The frailty syndrome total score ranges from 0 to 5. Scores below 3 indicate no frailty, scores between 3 and 5 imply pre-frailty, and a score of 6 or more suggests frailty[17].

The reduction in the HGS was evaluated in kilograms with a hydraulic dynamometer (Saehan Corporation, SH5001). The cutoff points considered both the BMI and the sex of the individual.

To assess physical activity, we used the condensed version of the International Physical Activity Questionnaire (IPAQ), with a cutoff of 150 minutes of vigorous physical activity per week to be classified as non-sedentary. Exhaustion was evaluated by two questions on the scale Center for Epidemiological Studies (CES-D): "I felt that I had to make an effort for the usual tasks" and "I could not carry on with my things"[17].

In the evaluation of sarcopenia, the criteria of the European Working Group on Sarcopenia in Older People[16] were considered, where the patient can be classified as having muscle mass reduction and presarcopenia; a reduction of muscle mass associated with loss of muscle strength or changes in physical performance and sarcopenia; or a loss of muscle mass associated with decreased strength and low physical performance and severe sarcopenia. Muscle mass was estimated using the Biodynamics 310e bioimpedance device, which was validated for this activity[18,19].

The equation for the calculation of lean mass with the data obtained was proposed in the literature: muscle mass (kg)= [(h^2/rx 0.401) + (sx 3.825) + (ix -0.071)] + 5.102. The letter "h" represents the height in cm; "R" is resistance in Ohms; "S" refers to sex (zero for women, one for males); and "I" is age in years. The muscle mass index (MMI) was calculated using the formula "muscle mass/height²", with height in meters; the cutoff point was <6.75 kg/m² for females and <10.75 kg/m² for males[20]. Muscle function was evaluated by strength through the PP results, and physical performance was evaluated through the HGS evaluation.

Statistical analysis

To characterize the sample, the mean, median, standard deviation, minimum, and maximum values were used. The normality of the data was verified by the Kolmogorov–Smirnov test. Among the variables, the viral load in the diagnosis was transformed into a square root to meet the assumptions of the analyses used. The Pearson correlation coefficient was used to verify the relationship between the independent variables and the IHDS. The independent variables with a p-value <0.20 in the correlation analysis were included in the simple linear regression models. However, only variables with $p<0.05$ after adjustment for the other independent variables were maintained in the final model (multivariate). All analyses were performed using the statistical software SPSS 25.0 (Armonk, NY).

RESULTS

Of all HIV patients over 50 years old who resided in Francisco Beltrão (n=72), 68.57% (n=48) participated in our study; 30.55% had spontaneous refusal (n=22), and 2.77% (n=2) were excluded because they were bedridden at the time of data collection. The sample consisted of 64.58% (n=31) white and 35.42% (n=17) black or brown individuals. Of the PLWH participants, 60.41% were females (n=29), and 58.3% were single (n=14) or divorced (n=14). About monthly income, 36.7% received up to R$1,100, and 20.4% had a monthly income equal to or over R$3,300 (Brazilian currency). Table 1 shows the typical characteristics of the sample.

Regarding the laboratory evaluation of patients, according to the current count ≤ 350 CD4+ T cells/mm^3, 18.75% of the patients interviewed (n=9) were present, and 89.58% of the participants had an undetectable VL (n=43). There was a moderate negative correlation between VL at diagnosis and CD4+ T cells at diagnosis, r= -0.345 (p=0.015). A total of 58.3%

of the participants were normoglycemic (*n*=28), and 37.5% (n=18) of the participants were diagnosed with dyslipidemia.

Approximately 45.83% of patients had changes in body composition by BMI: thinness 12.5% (n=6) or overweight 33.3% (n=16). A total of 50% of participants had reduced MMI (n=24), and of these individuals, 58.3% met the criteria for presarcopenia (n=14). Prefrailty was present in 39.58% of the participants (n=19). Regarding the level of physical activity, 72.91% (n=35) of the participants were classified as non-sedentary.

In the mental health assessment, 20.83% (n=10) of the participants were found to be at risk for depression. Regarding the neurocognitive evaluation, 75% had neurocognitive impairment according to the IHDS (n=36), 88.89% (n=32) were classified as having asymptomatic neurological infections (ANIs), and the other 11.11% (n=4) were classified as having mild/moderate neurological disorders (MNDs).

Table 2 shows the correlation and regression analyses of the independent variables studied with the IHDS. IHDS scores were positively correlated with educational level, MNA, and VL at diagnosis and negatively correlated with the number of diseases, number of medications, and blood glucose levels. However, education, VL at diagnosis, and blood glucose remained the main predictors in the final model, combining to explain 46% of the variance in IHDS.

DISCUSSION

Validated neuropsychological tests are the main method used in HAND screening due to their easy applicability, low cost, and high sensitivity. The IHDS[21] is internationally validated for use among PLWH and is the most widely used scale for screening neurocognitive disorders in this population[22-24]. Therefore, we chose this tool to screen for HANDs in our

study. We also used the IADL scale[25], which is the most commonly used instrument for assessing the degree of cognitive impairment of PLWH identified in neuropsychological evaluation[22,26].

Using the IHDS criteria, 75% of the sample met the criteria for HAND. Similar results were found in another research in Southern Brazil, in which 73% of PWLH ≥ 50 years showed neurocognitive alteration when solely the IHDS criteria was adopted[27]. Importantly, participants from Pinheiro et al.[27] study had comparable characteristics to our sample, including most white participants, close values for age, education, and even for the IHDS scores. Another study conducted in China - also with an elderly population – indicated high HAND prevalence (i.e., 87.2%)[6]. The higher frequency of HAND in the Chinese study might be explained by the fact that the average age was higher when compared to the current study.

It is well known that HIV exacerbates cognitive deficits related to aging due to the chronic inflammatory condition, thus making it a risk factor for cognitive impairment. The data regarding the frequency of HAND in PWLH ≥50 years found in our sample corroborates current studies that relate the aging process with a higher prevalence of cognitive dysfunction. Indeed, as age advances, there are natural developments in the neurocognitive functions, with a significant decrease in performance as people get older; moreover, in PLWH, these changes become more evident after 50 years[4,5].

It might also be highlighted that our data are in line with what has been discussed in the literature about the high prevalence rates of cognitive impairment in PLWH, thus stressing a relevant issue for public health[3,6,22-24,26,28-31]. Other Brazilian studies reported similar frequencies of HANDs, such as the studies conducted in the municipality of São Paulo[32] and in Florianópolis[22] that reported prevalence of 73.50% and 69.60%, respectively. In Fortaleza, another Brazilian municipality, a lower prevalence (41.60%) of HANDs was found[33], similar

to the prevalence of 45% found in Uruguay, another Latin American country[3]. It is important to note that these differences are due to variations in clinical and sociodemographic aspects as well as the variations in the tools used for HAND screening among the investigated populations.

Regarding the clinical forms of HAND, 88.89% of the participants were classified as having ANIs, and the remaining 11.11% were classified as having MNDs. HADs were not observed in our population. These data are consistent with the current literature, highlighting that even if viral suppression due to medication cannot prevent the occurrence of HANDs, and due to the advent of ART, there was a significant decrease in the prevalence of dementia that resulted from the improved health status and prognosis of PLWH[24,29,30,33,34]. ANIs are the most common types of HANDs[24,34,35]. In sum, several studies point to a higher risk of developing HAND in older patients[27,36]; however, in our sample, this finding was not replicated.

Our patients were using ART, indicating that despite the positive effects of the therapy, the medication cannot prevent the development of neurocognitive changes[3,24,28,29,31,37]. ARV enables peripheral viral suppression, and 89.58% of our participants had an undetectable viral load; however, this aspect did not reduce the risk of changes in the cognitive domain, given that the undetectable viral levels in the plasma do not necessarily reflect the amount of HIV in the CSF[3,22,34]. The presence of cognitive changes in PLWH, even those with an undetectable viral load, can be explained by the viral amount isolated in the CNS, the presence of irreversible brain lesions before starting ARV, or the inflammation caused by HIV[3,33].

Another point to consider is that even in regimens that include drugs with better penetration into the CNS, the literature indicates that there is no clinical improvement of HANDs; this was supported by our findings, reinforcing the hypothesis that irreversible neurological damage could be related both to the time of infection and the onset of ARV

regarding the systemic chronic inflammatory condition caused by the infection[6,28,29]. However, studies with more detailed analyses are necessary. It should also be noted that studies have indicated that the use of ARV with high penetration into the CNS was also a risk factor for HANDs, possibly due to its potential neurotoxicity[31,35,38].

An intriguing finding in our study was that VL diagnosis was positively related to IHDS values, including in the final linear regression model. However, the correlation between VL at diagnosis and CD4+ T cells at diagnosis showed that the higher the VL was, the lower the CD4+ T-cell value, thereby further compromising the immune system. Notably, an adequate level of CD4+ T cells is a protective factor against HANDs, demonstrating that the importance of immune balance is linked to its regulatory mechanisms that can attenuate neurodegeneration and cognitive impairment. Given this result, it was hypothesized that individuals with higher VL at diagnosis could be in the acute phase of infection, and once an early diagnosis has been made and ARV has been introduced, there was a decrease in CNS exposure to HIV and, therefore, less neurodegeneration. However, this hypothesis cannot be confirmed by our data and deserves further research.

It is also noteworthy that in our study, the CD4+ T-cell count was not related to cognitive performance, similar to other studies conducted in Brazil[22] and Kenya[29]. With the reduction in CD4+ T cells and the advancement of infection, there is a greater risk of cognitive impairment because VL may be increased not only in plasma but also in cerebrospinal fluid, promoting neurodegeneration. In more advanced stages, there is greater vulnerability to opportunistic infections and viral replication in multiple brain regions, which intensifies damage to brain tissue, acting mutually in the development of HAND[23,28,29]. Among the AIDS patients in our sample, 88.89% had cognitive impairment; in other studies, cognitive impairment was present in 71.80% of patients, which could suggest a relationship between

AIDS and HANDs[28]. However, there was no statistical significance between these variables in our study.

There was a negative correlation between the number of medications and diseases and the IHDS score in our sample. Studies have indicated the importance of screening and treatment of comorbidities in PWLH, especially those with relevant influences on cognition, such as neuropsychiatric diseases, and discouraging the use of drugs, aiming mainly to improve the health status of the individual and consequently the delay of the installed cognitive impairment or less potentiation of its occurrence[3,30].

Glycemia was also inversely related to IHDS, including in the final linear regression model, being a different finding in studies on HAND, more particularly in Latin America where this variable was not considered or did not obtain statistical relevance in the studies performed[3,22,32,33]. It is known that high blood glucose levels cause endothelial changes and are associated with neurocognitive impairment[39], with implications especially in older people due to the higher frequency of the development of cognitive disorders.

Insulin resistance (IR) participates in the development of beta-amyloid plaques and neurotoxic protein deposits due to the increase in oxidative oxygen species by hyperinsulinemia, promoting neuroinflammation and presenting itself as a risk factor. Given the possible outcomes related to blood glucose, we emphasize the need for further research on the mechanisms between blood glucose and HANDs.

The level of education of our participants also proved to be one of the main predictors of HANDs in the final multivariate model, being positively related to IHDS scores. Cognitive reserve, which is mainly linked to educational level, is one of the most important protective factors against HANDs[3,6,22,24,28–31,34,37,38] because it is associated with improved neural resources such as brain metabolism and synaptic communication, decreased cerebral atrophy,

and delayed neurocognitive impairment[22]. Low education is also associated with greater cognitive and functional decline, evidenced by lower scores on neurological tests, lower consistency in clinical follow-up, and lower adherence to HIV treatment[3,28,29].

The mini-nutritional assessment used in our sample was also positively related to cognitive performance, which is also a unique result, as previous studies examining HANDs did not present more complete nutritional assessments in PLWH. Malnutrition generates immune deficits, which may be influenced by vitamin deficiency, especially B12 deficiency[40] and other B vitamin deficiencies.

Although current studies indicate that females may have a higher risk of developing HANDs than males[6,22,24,29], there were no relationships between lower cognitive performance and sex in our sample. Another variable that did not have a significant relationship with cognitive performance was the presence of depressive symptoms, although numerous studies have shown that patients with depression are more likely to have HANDs[3,24,28,38]. Other variables, such as sarcopenia, frailty syndrome, level of physical activity, and duration of HIV infection, were not statistically significant in our study.

Although the consequences of HANDs on the health of PLWH are relevant, the screening of these changes is not part of the daily care of this population. In most services, including the health unit where our study was conducted, screening for cognitive impairment is not part of the routine, although several guidelines indicate the importance of neurological evaluation in PWLH[3,6,24,31]. It is important to note that HANDs hinder adherence to ARVs, bringing important health risks with the possibility of a negative clinical evolution in the patient, culminating in the worsening of disease[28,37].

Therefore, the early detection of HANDs should be included in the routine of PWLH care to improve the prognosis of these patients[3,30]. We should also consider that neurocognitive

disorders are public health problems that are more prevalent in PWLH than in the general population[6,28,31,37]; furthermore, these disorders are associated with a higher risk of mortality[37]. Early onset of ARV is essential for maintaining health status and improving immunity in patients, thereby avoiding premature neurodegeneration and the development of more severe forms of HAND[3,30].

It is necessary to highlight that our research has some limitations: (a) because it was a cross-sectional study, we could not establish causality and only infer associations; (b) we performed a brief HAND screening with internationally validated scales; however, we could not establish the diagnosis because it would require a complete neuropsychological evaluation by a specialist; (c) due to the small sample of our study and because it was a convenience sample, selection bias may have affected our results, and it is not possible to generalize the results reported herein; and (d) our sample was predominantly white, which may not allow the reproduction of our findings in more heterogeneous populations.

In conclusion, HANDs were associated with lower educational levels, VL at diagnosis, and blood glucose; other variables, such as nutritional status, number of medications, and comorbidities, may also explain the development of HANDs. Also, the IHDS, in addition to having easy applicability, high sensitivity, and affordability, proved to be useful as a screening tool for HANDs; however, the authors argue that complete neuropsychological evaluation by a specialist is still the best way to diagnose HANDs.

Despite the relevance of this topic, neurocognitive assessment is not a routine in most services that serve PWLH. Early diagnosis of HAND is important for a better prognosis of the patient. The immediate initiation of ARV after diagnosis of HIV, the screening and treatment of comorbidities, and discouragement of drug use are also necessary interventions for a more positive prognosis.

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Table 1: Typical characteristics of the sample (n=48).

Variable	Mean	Median	Standard deviation	Minimum	Maximum
Age (years)	59.6	57.5	6.9	51	72
Age at diagnosis (years)	50.3	51.0	9.1	28	66
Scholarity (years)	7.5	7.5	4.6	0	20
Comorbidities (n)	1.7	1.0	1.4	0	5
Medicines (n)	2.4	2.0	2.0	0	9
MNA	26.0	26.3	3.1	17	30
CD4+ T cells at diagnosis (cells/mm ^{3})	399.9	377.5	313.8	27	1,758
Current CD4+ T cells (cells/mm ^{3})	561.5	531.0	256.1	84	1,112
VL at diagnosis (copies/ml)	250,024	34,416	482,914	39	2,374,923
Current VL (copies/ml)	29,241	39	200,586	39	1,389,960
Glycemia (mg/dL)	105.3	98.5	29.1	77	245
Total cholesterol (mg/dL)	203.7	201.0	47.0	101	330
HDL (mg/dL)	49.4	47.0	18.1	10	99
Triglycerides (mg/dL)	176.0	147.0	114.9	54	643
LDL (mg/dL)	121.8	110.5	34.5	65	220
BMI (kg/m^2)	25.9	25.8	4.4	16.1	35.6
MMI (kg/m^2)	8.4	8.0	1.7	5.5	12.1
Gait speed (m/s)	0.88	0.89	0.19	0.41	1.34
IHDS	*8.4*	*8.5*	*2.0*	*2.5*	*12.0*

MNA: mini nutritional assessment; VL: viral load; HDL: high-density lipoprotein; LDL: low-density lipoprotein; BMI: body mass index; MMI: muscle mass index; IHDS: International HIV Dementia Scale

Table 2: Correlation between the independent variables and the IHDS and crude and adjusted linear regression models with the main factors associated with the outcome.

	Pearson correlation		**Linear regression**			
	r	***p***	**β_{BR} (IC 95%)**	***p***	**β_{AJ} (IC 95%**	***p***
Age (years)	-0.249	0.084	-0.07 (-0.16; 0.01)	0.084	---	---
Age at diagnosis (years)	-0.180	0.216	---	---	---	---
Scholarity (years)	0.436	0.002	0.19 (0.08; 0.31)	0.002	0.21 (0.11; 0.30)	< 0.001
Comorbidities (n)	-0.285	0.047	-0.41 (-0.80; -0.01)	0.047	---	---
Medicines (n)	-0.298	0.037	-0.30 (-0.58; -0.02)	0.037	---	---
MNA	0.353	0.013	0.23 (0.05; 0.41)	0.013	---	---
CD4+ T cells at diagnosis (cells/mm ^{3})	-0.274	0.057	-0.002 (-0.004; 0.000)	0.057	---	---
Current CD4+ T cells (cells/mm ^{3})	-0.058	0.694	---	---	---	---
VL at diagnosis (copies/ml) *	0.356	0.012	0.002 (0.000; 0.003)	0.012	0.002 (0.001; 0.003)	0.001
Current VL (copies/ml)	0.040	0.784	---	---	---	---
Glycemia (mg/dL)	-0.333	0.019	-0.02 (-0.04; -0.01)	0.019	-0.02 (-0.04; -0.01)	0.003
Total cholesterol (mg/dL)	0.022	0.880	---	---	---	---
HDL (mg/dL)	-0.199	0.171	-0.02 (-0.05; 0.01)	0.171	---	---
Triglycerides (mg/dL)	0.108	0.462	---	---	---	---
LDL (mg/dL)	0.042	0.774	---	---	---	---
BMI (kg/m^2)	0.055	0.708	---	---	---	---
MMI (kg/m^2)	0.195	0.185	0.23 (-0.11; 0.57)	0.185	---	---
Gait speed (m/s)	0.283	0.052	2.92 (-0.02; 5.86)	0.052	---	---

MNA: mini nutritional assessment; VL: viral load; HDL: high-density lipoprotein; LDL: low-density lipoprotein; BMI: body mass index; MMI: muscle mass index; IHDS: International HIV Dementia Scale. *Variable transformed by square root. The raw models are composed of the variables that presented p <0.20 in the correlation analyses. Only the coefficients of the variables with p <0.05 are shown in the adjusted analysis.