

### Nutrición Hospitalaria



## Trabajo Original

Valoración nutricional

# 25(OH)D concentrations are not associated with adiposity indicators, but with the stage of immunodeficiency in people with HIV/AIDS

Las concentraciones de 25(OH)D no se asocian con los indicadores de adiposidad, pero sí con el estadio de inmunodeficiencia en personas con VIH/SIDA

Andrea Nunes Mendes de Brito<sup>1</sup>, lara Katrynne Fonsêca Oliveira<sup>1</sup>, Nayra do Socorro Caldas Carvalho de Almeida Teixeira<sup>1</sup>, Dorcas Lamounier Costa<sup>2</sup>, Poliana Cristina de Almeida Fonseca<sup>1</sup>, Patrícia Helen de Carvalho Rondó<sup>3</sup>, Liania Alves Luzia<sup>3</sup>, Isabel Oliveira Aires<sup>3</sup>, Adriana de Azevedo Paiva<sup>1</sup>

<sup>1</sup>Nutrition, and <sup>2</sup>Mother and Child Health Departments. University Federal of Piauí. Teresina, Piauí. Brazil. <sup>3</sup>School of Public Health. University of São Paulo. São Paulo, Brazil

### Abstract

**Objective:** this study assessed the association between serum 25(OH)D concentrations and anthropometric indicators of adiposity in people living with HIV/AIDS taking highly active antiretroviral therapy.

**Methods:** the study included 244 people living with HIV/AIDS who received outpatient care at the Institute of Tropical Diseases in the city of Teresina, Brazil. Sociodemographic, clinical, anthropometric and laboratory characteristics were examined. Serum 25(OH)D was analyzed by high-performance liquid chromatography in accordance with the Vitamin D Standardization Program. Multiple linear regression analysis adjusted for gender, age, disease stage and duration of highly active antiretroviral therapy was performed to assess the association between 25(OH)D concentrations and adiposity indicators.

**Results:** the study included 142 (58.2 %) men and 102 (41.8 %) women, with a mean ( $\pm$  SD) age of 39.13 ( $\pm$  10.83) years. A proportion of 57.8 per cent of the participants had insufficient concentrations of 25(OH)D below 30 ng/mL. Individuals in more advanced stages of immunodeficiency had lower concentrations of 25(OH)D (30.30  $\pm$  16.10 ng/mL) compared to those with mild immunodeficiency or no immunodeficiency. There was no significant association between 25(OH)D concentrations and any of the adiposity indicators considered in this study.

### Keywords:

Vitamin D. Anthropometric indicators. Adiposity. Immunosuppression. HIV.

**Conclusion:** vitamin D concentrations in people living with HIV/AIDS using antiretroviral therapy are related to the degree of immunosuppression, but not to the individual's adiposity status.

Received: 16/03/2024 • Accepted: 02/12/2024

Source of funding: Fundação de Amparo à Pesquisa do Estado do Piauí (Edital nº 002/2016- PPSUS, 2016), Ministério da Saúde- DECIT, CNPq and Secretaria de Saúde do Estado do Piauí- SESAPI.

Ethical responsibilities: the Human Research Ethics Committee of the Federal University of Piaui approved the study (No. 2, 100, 110 June 5th, 2017). The study was registered in the Brazilian Registry of Clinical Trials (REBEC) UTN U111-1247-3745 and RBR- 5h432f (https://ensaiosclinicos.gov.br/).

Conflict of interest: the authors declare no conflict of interest.

Artificial intelligence: the authors declare not to have used artificial intelligence (AI) or any AI-assisted technologies in the elaboration of the article.

Brito ANM, Oliveira LKF, Teixeira NSCCA, Costa DL, Fonseca PCA, Rondó PHC, Luzia LA, Aires IO, Paiva AA. 25(OH)D concentrations are not associated with adiposity indicators, but with the stage of immunodeficiency in people with HIV/AIDS. Nutr Hosp 2025;42(1):89-96

#### Correspondence:

Andrea Nunes Mendes de Brito. Universidade Federal do Piauí. Campus Universitário Ministro Petrônio Portella-Ininga, Teresina. Piaui, Brasil e-mail: drea.nunes@hotmail.com

DOI: http://dx.doi.org/10.20960/nh.05288

Copyright 2025 SENPE y Cara Ediciones S.L. Este es un artículo Open Access bajo la licencia CC BY-NC-SA (http://creativecommons.org/licenses/by-nc-sa/4.0/).

#### Resumen

**Objetivo:** este estudio evaluó la asociación entre las concentraciones séricas de 25(OH)D y los indicadores antropométricos de adiposidad en personas que viven con VIH/SIDA y toman terapia antirretroviral de gran actividad.

**Métodos:** el estudio incluyó a 244 personas viviendo con VIH/SIDA que recibían atención ambulatoria en el Instituto de Enfermedades Tropicales de la ciudad de Teresina, Brasil. Se examinaron las características sociodemográficas, clínicas, antropométricas y de laboratorio. La 25(OH)D sérica se analizó mediante cromatografía líquida de alta resolución de acuerdo con el Programa de Estandarización de la vitamina D. Se realizó un análisis de regresión lineal múltiple ajustado por sexo, edad, estadio de la enfermedad y duración del tratamiento antirretroviral de gran actividad para evaluar la asociación entre las concentraciones de 25(OH)D y los indicadores de adiposidad.

**Resultados:** en el estudio participaron 142 (58,2 %) hombres y 102 (41,8 %) mujeres, con una edad media (± DE) de 39,13 (± 10,83) años. El 57,8 % de los participantes presentaba concentraciones insuficientes de 25(OH)D inferiores a 30 ng/mL. Los individuos en estadios más avanzados de inmunodeficiencia presentaban concentraciones más bajas de 25(OH)D (30,30 ± 16,10 ng/mL) en comparación con aquellos con inmunodeficiencia leve o sin inmunodeficiencia. No se observó ninguna asociación significativa entre las concentraciones de 25(OH)D y ninguno de los indicadores de adiposidad considerados en este estudio.

**Conclusiones:** las concentraciones de vitamina D en personas que viven con VIH/SIDA y utilizan terapia antirretroviral están relacionadas con el grado de inmunosupresión, pero no con el estado de adiposidad del individuo.

#### INTRODUCTION

Individuals living with human immunodeficiency virus/AIDS (PLWHA) typically experience a reduction in serum 25(OH)D concentrations. This decrease is linked with infections and metabolic alterations, leading to immune system dysfunction, lower CD4 T lymphocyte (TCD4+) counts, rapid disease progression, and decreased survival time (1).

In 2022, the United Nations data on HIV/AIDS (UNAIDS) estimated that 39 million people were living with the virus, and about 630 thousand people died from AIDS-related diseases worldwide (2). In Brazil, the number of cases of HIV infection declined by 11.1 % between 2019 and 2021. The COVID-19 pandemic has had a major impact on AIDS notifications and contributed to a 20.1 % drop in registrations when comparing 2019 and 2020. In 2021, the national AIDS detection rate was 16.5 cases per 100,000 inhabitants, and Teresina city, Brazil, had 19.9 cases per 100,000 inhabitants, ranking fifteenth among the Brazilian federal units (3).

The Brazilian Health Ministry (BHM) recommends utilizing highly active antiretroviral therapy (HAART) as the fundamental treatment protocol for HIV, which should encompass three combined antiretroviral drugs (4). Advancements in HAART can indubitably enhance the quality of life of people living with HIV/ AIDS by suppressing viral replication and increasing longevity, ultimately resulting in a significant reduction in opportunistic infections and associated fatalities (5).

However, HAART may lead to several unfavorable outcomes, including certain serious metabolic and lipid disorders like lipodystrophy, and an increased risk of cardiovascular diseases. This alteration is due to the duration of therapy, which changes the distribution of fat and lean mass in the body with varying percentages (6,7).

HAART also influences serum 25(OH)D concentrations, predisposing to vitamin D deficiency or insufficiency (8). The causes of vitamin D deficiency in HIV infections include HIV itself, traditional factors such as less sun exposure, malabsorption, hypercholesterolemia, seasonal variation, poor nutrition, as well as some HAART drugs such as efavirenz. Vitamin D has an immunomodulatory, anti-inflammatory and anti-proliferative action (9). Another significant impact of Vitamin D in PLWHA is its influence on their body mass index (BMI), as adipocytes require higher levels of vitamin D concentration to be stored properly (10). However, the clinical significance of vitamin D insufficiency for people living with HIV/AIDS is unclear, as few studies have explored the correlation between vitamin D and disease development, as well as its link with anthropometric indicators and global health markers (11). Consequently, this study seeks to evaluate the associations between serum 25(OH)D concentrations and anthropometric indicators of adiposity among PLWHA receiving antiretroviral therapy.

#### **METHODS**

#### STUDY DESIGN AND PARTICIPANTS

Cross-sectional study involving PLWHA, registered at the Specialized Care Service (SCS), in outpatient care at the Institute of Tropical Diseases "Natan Portela" (ITDNP), a reference hospital for monitoring people living with HIV/AIDS in the Northeast of Brazil.

A total of 244 PLWHA took part in the study. Considering 36 % of vitamin D deficiency (12), the power of the sample was 90 %. The patients were selected for convenience according to a routine consultation schedule at the clinic, from august 2017 to June 2018. The inclusion criteria were participants enrolled in the SCS; living in Teresina city; 20 years of age or older; fasting for 12 hours; not using vitamin supplementation; not having metabolic diseases (diabetes, metabolic syndrome, thyroid disorders), bone diseases, chronic renal failure, liver disease, gastric diseases or disabsorptive syndromes, cancer or pregnant and lactating women. The Human Research Ethics Committee of the Federal University of Piaui approved the study (No. 2,100,110 June 5<sup>th</sup>, 2017). The study was registered in the Brazilian Registry of Clinical Trials (REBEC) UTN U111-1247-3745 and RBR- 5h432f (https://ensaiosclinicos.gov.br/).

#### DATA COLLECTION

Clinical data was collected using a specific form, and medical records were assessed as necessary. Demographic variables

Palabras clave: Vitamina D. Indicadores antropométricos. Adiposidad. Inmunosupresión. VIH were collected, including gender, age and self-reported skin color, as well as socioeconomic variables such as education, financial income and lifestyle habits (alcohol consumption, current smoking, frequency of sunscreen use and spending time under sun light). Income was reported as a quantitative variable in the Brazilian currency (Real; R\$).

The anthropometric variables weight (kg), height (m), waist circumference (cm), neck circumference (cm) and triceps skinfold (mm) and subscapular skinfold (mm) were measured. TCD4+ cell count (cells/mm<sup>3</sup>) and serum 25(OH)D concentrations (ng/mL) were also evaluated.

Body weight was measured on a Seca<sup>®</sup> digital scale, with a capacity of 180 kg and accuracy of 100 g, with the patient barefoot and wearing light clothing. The height was determined on a portable vertical stadiometer, Seca<sup>®</sup> brand, with a 2.20 m ruler and 1.0 cm precision (13). Based on the ratio between weight (kg) and the square of height (m), body mass index (BMI) was calculated, and the following cut-off points were adopted for classifying nutritional status: BMI < 18.5 kg/m<sup>2</sup>: underweight; BMI  $\geq$  18.5 and < 25 kg/m<sup>2</sup>: eutrophic; BMI  $\geq$  25 and < 30 kg/m<sup>2</sup>: overweight; BMI  $\geq$  30 kg/m<sup>2</sup>: obses. In the association analyses, participants were categorized as non-obses < 30 kg/m<sup>2</sup> and obses  $\geq$  30 kg/m<sup>2</sup> (13).

Waist circumference (WC) was measured on the umbilical scar using a Seca<sup>®</sup> inelastic tape, with a capacity of 1.5 m and an accuracy of 0.1 cm. The cutoff points used were  $\geq$  80 cm for females and  $\geq$  94 cm for males according to WHO (14). For neck circumference (NC) the cutoff points used were  $\geq$  39 cm for males and  $\geq$  35 cm for female (14). Anthropometric measurements were measured in triplicates and the mean was used for calculations.

Based on anthropometric measurements, the waist-to-height ratio (WHTR) was also calculated (15) and the taper index (TI) was determined from the mathematical equation proposed by Valdez (16).

For classification of the WHTR, a cut-off point was defined as  $\geq$  0.5 for both genders, which represents the best balance between sensitivity and specificity, indicating that WHTR greater than 0.5 is related to higher cardiovascular risk (17). For the TI, the cutoff points were  $\geq$  1.25 and  $\geq$  1.18 for males and females, respectively, based on the study of Pitanga & Lessa (18,19).

Skinfold were measured using a LANGE<sup>®</sup> adipometer, with 1 mm accuracy. The triceps skinfolds (TS) reading was performed on the posterior face of the right arm, parallel to the longitudinal axis, at the midpoint between the acromion and the olecranon. The subscapular skinfold (SS) measurement was performed on the individual's right side, two centimeters below the lower scapula angle (20).

#### **BIOCHEMICAL ANALYSIS**

Two blood samples were collected for each patient. One sample was collected for TCD4+ lymphocyte count, and the other sample was collected for vitamin D analysis. Both samples were collected on the same day.

The TCD4+ lymphocyte count was performed at the Central Laboratory of Public Health of the State of Piaui (CLPH-PI) and the results were obtained by the SCS electronic medical record at ITDNP. Flow Cytometry (BD TrucountTM Tubes) was used to quantify T lymphocytes, using the FACS Calibur device (Becton-Dickinson, New Jersey, USA).

The 25(OH)D analysis was performed by High Performance Liquid Chromatography (HPLC) at the Micronutrient Laboratory of the Faculty of Public Health at the University of São Paulo, according to the Vitamin D Standardization Program, using the methodology proposed by Neyestani et al. (21) with adaptations. Vitamin D insufficiency (VDI) was considered when serum concentrations of 25(OH)D were < 30 ng/mL (22).

#### **DISEASE STAGE**

The classification of the disease stage was performed according to the last evaluation of TCD4+ lymphocytes count. PLWHA without immunosuppression or early immunosuppression have TCD4+ lymphocytes above 500 cells/mm<sup>3</sup>, which is characterized by increased energy expenditure and changes in vitamins and minerals storage. PLWHA with TCD4+ lymphocyte values between 350 to 500 cells/mm<sup>3</sup> are considered as having mild or intermediate immunodeficiency, characterized by association with nutritional deficiencies, fluctuating food intake cycle (times of feeding and lack of appetite) and greater susceptibility to infections. Finally, PLWHA with TCD4+ lymphocyte values less than 350 cells/mm<sup>3</sup> are in a late or advanced immunodeficiency, characterized by an increased risk for severe and intractable weight loss, resulting in malnutrition and chronic fatigue, in addition to occurrences of acute and/or chronic enteropathies and more frequently acute infections.

#### STATISTICAL ANALYSIS

Data analysis was performed using the STATA<sup>®</sup> version 13.0, Stata Corporation, College Station, Texas (23). The normality was assessed by the Shapiro-Wilk normality test. Serum 25(OH) D concentrations were expressed as means  $\pm$  standard deviation (SD) and Student's t test and one-way ANOVA were used to compare explanatory variables. To analyse the association of anthropometric indicators with serum vitamin D concentrations, a multiple linear regression model was used with adjustment for gender, age, disease stage and duration of HAART. For all statistical tests, values of p < 0.05 were established as significant.

#### RESULTS

The study included 142 (58.2 %) men and 102 (41.8 %) women, with a mean ( $\pm$  SD) age of 39.13 ( $\pm$  10.83) years. The prevalence of VDI (< 30 ng/ml) in the study population was 57.8 %. When assessed by gender, men had a higher NC mean, while women had higher TS, WHTR and TI mean values. It is noteworthy that the BMI means for both genders were close to the upper limit of normal weight (Table I).

Our results showed a high prevalence of vitamin D insufficiency in the population studied, with a mean (SD) concentration of 34.29 ng/ml (16.89 ng/mL) (data not shown in the table). When vitamin D concentrations were analysed in relation to the sociodemographic, clinical and lifestyle characteristics of the individuals, it was observed that PLWHA in advanced stages of immunodepression had significantly lower 25(OH)D values [mean (SD) 30.30 ng/mL ( $\pm$  16.10)] compared to people with mild immunodeficiency [37.89 ng/mL ( $\pm$  15.67)] and without detectable immunodeficiency [(35.63 ng/mL ( $\pm$  17.52)] ( $\rho$  < 0.022). For the other variables analysed, serum vitamin D concentrations showed no statistically significant differences (Table II).

In addition, a comparison of individuals without and with mild immunodeficiency [mean (SD)  $36.32 \text{ ng/mL} (\pm 16.96)$ ] with those who were severely immunodepressed [mean (SD) 30.30 ng/mL

 $(\pm 16.10)$ ] revealed that the 25[OH]D values remained statistically significant (p = 0.022) (data not shown in table).

A total of 54.2 % of the subjects were found to have a normal weight according to their BMI. Only 4.0 % were classified as underweight, while 31.8 % were identified as overweight and 10 % as obese. Consequently, 90 % of the sample was categorized as non-obese, as illustrated in table III. Moreover, 53.7 % of the subjects had a high cardiometabolic risk according to WC. There was no statistically significant difference in 25(OH) D levels concentrations in the different categories identified according to the adiposity indicators assessed in this study (p > 0.05) (Table III).

Multiple linear regression analysis with adjustment for the variables gender, age, stage of the disease and time on HAART confirmed the absence of an association between serum 25(OH) D concentrations and anthropometric indicators of adiposity in PLWHA included in this study. The results obtained with the proposed regression model are shown in table IV.

Variables	Mean (±SD) ( <i>n</i> = 244)	Mean (±SD) Mean (±SD)   Male(n = 142) Female (n = 102)		p value
Age (years)	39.13 (±10.83)	37.58 (±10.94)	41.28 (±10.34)	0.008
BMI (kg/m²)	24.32 (±4.03)	24.34 (±3.94)	24.27 (±4.17)	0.899
WC (cm)	85.37 (±10.85)	85.41 (±10.21)	85.32 (±11.73)	0.951
NC (cm)	35.36 (±3.98)	37.17 (±3.25)	32.82 (±3.48)	< 0.001
TS (mm)	13.83 (±6.75)	11.37 (±5.93)	17.25 (±6.36)	< 0.001
SS (mm)	16.52 (±6.54)	16.20 (±6.68)	16.96 (±6.34)	0.372
WHTR (cm/m)	0.52 (±0.07)	0.51 (±0.06)	0.54 (±0.07)	< 0.001
TI	1.25 (±0.14)	1.23 (±0.13)	1.27 (±0.15)	0.016

**Table I.** Mean values (standard deviations) of anthropometric indicators of adiposity stratified by gender in people living with HIV/AIDS (n = 244)

BMI: body mass index; WC: waist circmference; NC: neck circumference; TS: triceps skinfold; SS: subscapular skinfold; WHTR: waist to height ratio; TI: taper index. Student's t test.

Table II. Serum 25(OH)D concentrations according to sociodemographic, clinical
and lifestyle characteristics in people living with HIV/AIDS ( $n = 244$ )

Variables	n (%)	25 (OH)D ng/mL Mean (±SD)	<i>p</i> value	
Gender*				
Male	142 (58.2)	33.05 ± 16.31	0.173	
Female	102 (41.8)	36.03 ± 17.59		
Age range (years)**				
< 31 (young adults)	60 (24.6)	35.19 ± 15.53	0.817	
31-59 (adults)	173 (70.9)	34.14 ± 17.50		
> 59 (elderly)	11 (4.5)	31.88 ± 15.16		
Skin color*				
Caucasian	54 (22.1)	37.07 ± 17.48	0.171	
Not caucasian	190 (77.9)	33.5 ± 16.68		

(Continues on next page)

92

Nutr Hosp 2025;42(1):89-96

Variables	n (%)	25 (OH)D ng/mL Mean (±SD)	p value		
Income**					
Smallest tertile	105 (43.0)	34.49 ± 17.63	0.015		
Intermediate tertile	66 (27.0)	35.09 ± 18.52	0.815		
Largest tertile	73 (30.0)	33.30 ± 14.23	7		
Study years**					
< 9					
9 to 11	51 (20.9)	31.78 ± 16.96	0.074		
12 or more	130 (53.3)	36.60 ± 16.79			
Current smoker*					
No	206 (84.4)	34.32 ± 17.03	0.961		
Yes	38 (15.6)	34.17 ± 16.13			
Alcohol use*					
No	141 (57.8)	34.99 ± 18.41	0.453		
Yes	103 (42.2)	33.34 ± 14.58			
Sunscreen use*					
No	135 (55.3)	33.39 ± 16.76	0.351		
Yes	109 (44.7)	35.42 ± 17.06			
Spending time under sun light*					
≤ 60 min/day	188 (77.0)	33.44 ± 16.41	0.146		
> 60 min/day	56 (23.0)	37.17 ± 18.27			
Disease stage**					
No Immunodeficiency <sup>a</sup>	113 (46.3)	35.63 ± 17.52	0,999 <sup>a,b</sup>		
Light Immunodeficiency <sup>®</sup>	49 (20.1)	37.89 ± 15.67	0,086 <sup>a,c</sup>		
Advanced Immunodeficiency <sup>c</sup>	82 (33.6)	30.30 ± 16.10	0,037 <sup>b,c</sup>		
HAART duration*					
< 12 months	69 (28.27 %)	32.83 ± 14.66	0.397		
> 12 months	175 (71.72 %)	34.87 ± 17.79			

### Table II (cont.). Serum 25(OH)D concentrations according to sociodemographic, clinical<br/>and lifestyle characteristics in people living with HIV/AIDS (n = 244)

HAART: highly active antiretroviral therapy; \*Student's t test; \*\*ANOVA with Bonferroni test contrast.

# **Table III.** Serum 25(OH)D concentrations according to anthropometric indicators<br/>of adiposity in people living with HIV/AIDS (n = 244)

Variables	n (%)	25 OHD ng/mL Mean (±SD)	<i>p</i> value
BMI (kg/m²)			
Not obese (< 30)	222 (90.0)	34.63 ±17.04	0.331
Obese ≥ 30)	22 (10.0)	30.96 ± 15.27	
WC (cm)			
Low risk	113 (46.3)	32.74 ± 16.00	0.183
High risk	131 (53.7)	35.63 ± 17.57	
NC (cm)			
Low risk	176 (72.1)	33.64 ± 16.85	0.329
High risk	68 (27.9)	35.99 ± 16.98	

(Continues on next page)

Variables	n (%)	25 OHD ng/mL Mean (±SD)	<i>p</i> value		
TS (mm)					
Smallest tertile	89 (36.5)	34.50 ± 16.82	0.057		
Intermediate tertile	80 (32.8) 33.84 ± 1		0.957		
Largest tertile	75 (30.7)	34.54 ± 16.47			
SS (mm)					
Smallest tertile	89 (36.5)	33.41 ± 18.11	0.792		
ntermediate tertile	80 (32.8)	34.36 ± 17.21	0.792		
Largest tertile	75 (30.7)	35.19 ± 15.31			
WHTR (cm/m)					
Low risk	132 (52.8)	33.85 ± 17.08	0.661		
High risk	118 (47.2)	34.80 ± 16.72			
71					
Low risk	106 (43.4)	33.64 ± 16.86	0.329		
High risk	138 (56.6)	36.00 ± 16.98			

### Table III (cont.). Serum 25(OH)D concentrations according to anthropometric indicatorsof adiposity in people living with HIV/AIDS (n = 244)

BMI: body mass index; WC: waist circumference; NC: neck circumference; TS: triceps skinfold; SS: subscapular skinfold; WHTR: waist to height ratio; TI: taper index. \*Student's t test.

Verieklee	Raw analysis		Ajusted <sup>†</sup>			
Variables	В	<i>p</i> value	IC95 %	В	<i>p</i> value	IC95 %
BMI (kg/m²) Obese	-3.67	0.332	(-11.11-3.67)	-4.41	0.242	(-11.84-3.00)
WC (cm) Risk	2.88	0.184	(-1.38-7.15)	3.60	0.098	(-1.38-7.15)
NC (cm) Risk	2.36	0.329	(-2.39-7.11)	1.73	0.482	(-3.10-6.55)
<i>TS (mm)</i> Intermediate tertile Largest tertile	-0.66 0.04	0.800 0.989	(-5.81– 4.48) (-5.20– 5.27)	-1.62 -1.50	0.551 0.604	(-6.97-3.72) (-7.28-4.28)
<i>SS (mm)</i> Intermediate tertile Largest tertile	0.95 1.78	0.720 0.498	(-4.27-6.17) (-3.40-6.96)	1.11 1.11	0.675 0.674	(-7.28-4.28) (-4.09-6.31)
WHTR (cm/m) Risk	0.95	0.662	(-3.32-5.22)	-0.64	0.778	(-4.09-6.31)
<i>TI</i> Risk	0.61	0.779	(-3.69-4.92)	-1.20	0.610	(-5.85-3.44)

### **Table IV.** Association between serum 25(OH)D concentrations and anthropometricindicators of adiposity in people living with HIV/AIDS (n = 244).

BMI: body mass index; WC: waist circumference; NC: neck circumference; TS: triceps skinfold; SS: subscapular skinfold; WHTR: waist to height ratio; TI: taper index. Student's t test. †Multiple linear regression adjusted for gender, age, disease stage and antiretroviral therapy time.

#### DISCUSSION

This study included 244 individuals living with HIV/AIDS (PLWHA), and although their average 25(OH)D concentration was in the normal range (34.2 ng/ml), a high proportion (57.8 per cent) displayed vitamin insufficiency. These findings suggest that VDI may present a public health concern (24) among individuals with HIV, despite residing in a region near the equator, which affords year-round sunlight exposure and a low use of sunscreen (55.3 %) (25).

The study found that individuals with advanced immunodeficiency had lower levels of vitamin D in their serum, compared to those who were mildly immunosuppressed. This can be attributed to the effects of the HIV virus itself and antiretroviral drugs, which can lead to low levels of vitamin D. This suggests a possible link between the progression of the disease and nutritional deficiencies. However, there was no statistically significant difference in vitamin D levels between individuals without immunosuppression and those with mild immunodeficiency, possibly due to greater variability in vitamin D values in people without immunosuppression (26,27).

The molecular mechanism of vitamin D and its immunomodulatory actions may hold the key. Vitamin D inhibits Th-1 cell multiplication, resulting in lower levels of gamma interferon and interleukins. Furthermore, circulating cytokines are decreased, which leads to less antigen presentation by dendritic cells and reduced recruitment and proliferation of TCD4+ cells (28).

The required 25(OH)D concentration for adequate bone health is > 20 ng/mL in healthy individuals and 30 ng/mL in at-risk populations such as PLWHA (29,30). Studies indicate a high prevalence of hypovitaminosis D among PLWHA. However, some of them had normal blood concentrations, indicating a significant variety in vitamin D values among the studied population, which is also consistent with the findings of the present study (31,32).

In this context, studies in other populations around the world have suggested that vitamin D deficiency is common, but the variability is high, probably due to methodological diversity and different confounding factors. Vitamin D insufficiency (< 30 ng/ml) in adults has been shown to be quite high in Portugal (96.4 %) and in participants in the South Indian cohort (81 %) (33,34). In addition, meta-analyses of studies conducted in South America and South Asia found a prevalence of vitamin D insufficiency of 34.76 % and 68 %, respectively (35,36). This information highlights the need to critically evaluate the relevance of vitamin D deficiency as a public health problem for different groups, including PLWHA.

The prevalence of vitamin D deficiency (< 20 ng/ml) in PLWHA receiving antiretroviral treatment was also variable, with 51.3 % and 63.2 % of American and South Korean patients, respectively, being vitamin D deficient (38,39), results similar to those in this study. Vitamin D plays an important role in modulating the innate and adaptive immune systems, influencing the production of endogenous antimicrobial peptides and regulating the inflammatory cascade, which may influence susceptibility to HIV infection and response to antiretroviral treatment.

The study by Canuto et al. (40) identified an association between lower vitamin D values and the use of HAART, which may refer to both the type of antiretroviral therapy and the duration of treatment (p < 0.05), as well as overweight/obesity (p < 0.01). On the other hand, higher concentrations of vitamin D in the bloodstream were associated with females (p < 0.001). Similar results were discovered in the current research.

Vitamin D may play an important role in slowing HIV disease progression and reducing TCD4+ lymphocyte surface receptor expression in human monocytes and the promyelocytic leukemia cell line (41,42). Additionally, vitamin D deficiency may be linked to low TCD4+ lymphocyte count, lower BMI, less adiposity, and reduced lean mass indicating nutritional deficits (40).

Although few studies have examined the association between anthropometric indicators and adiposity with vitamin D in PLWHA, it is well established that HIV infection and subsequent immune deficiencies can lead to early weight loss. In contrast, research suggests that greater fat accumulation is linked to HAART usage and therapy duration, attributable to associated mitochondrial dysfunction (43,44). While our study did not reveal any statistically significant difference (p > 0.05) between the assessed anthropometric parameters and serum 25(OH)D concentrations, it is important to note that high levels of body fat can actually decrease one's serum vitamin D concentrations, as it is stored in fat cells. Therefore, monitoring anthropometric parameters, including waist circumference, neck circumference, skinfolds, and BMI, in these individuals can improve their quality of life and mitigate the negative effects of this condition (45). Using parameters that are more sensitive to body fat is recommended for better outcomes.

It is important to note that our study is the first of its kind to evaluate the association between anthropometric markers of obesity and HIV/AIDS infection in adults receiving antiviral therapy in a capital city in northeastern Brazil. Despite its relevance, the study is limited by the lack of a control group (not treated with HAART), which limits the evaluation of the effect of the disease and the treatment used. In addition, the lack of association between serum vitamin D concentrations and anthropometric indicators can be attributed to the sample size and the nutritional status of the participants, due to the low incidence of obesity.

Thus, no association was found between 25(OH)D concentrations and body adiposity among PLWHA on HAART. However, individuals with advanced immunodeficiency had lower serum vitamin D concentrations. This finding indicates that adiposity may have a lesser effect on vitamin D sequestration in PLWHA than in healthy individuals. In addition, the stage of immunosuppression has a greater impact on reducing blood concentrations of the vitamin. Future follow-up studies would be useful to further clarify the relationship between vitamin D, adiposity and immunosuppression in people with HIV receiving treatment.

#### REFERENCES

- Jiménez-Sousa Má, Martínez I, Medrano LM, Fernández Rodríguez A, Resino S. Vita- min D in Human Immunodeficiency Virus Infection: Influence on Immunity and Disease. Front Immunol 2018;9(1):11.
- UNAIDS, DATA; UPDATE, AIDS Epidemic. Geneva: Joint United Nations Programme on HIV. AIDS; 2022.

- BRASIL. Ministério da Saúde. Secretaria de Vigilância em Saúde. Departamento de Vigilância, Prevenção e Controle das Infecções Sexualmente Transmissíveis, do HIV/Aids e das Hepatites Virais. Boletim Epidemiológico HIV/Aids. Brasília, DF; 2021;49(53).
- 4. BRASIL. Ministério da Saúde. Protocolo Clínico e Diretrizes Terapêuticas para Manejo da Infecção pelo HIV em Adultos. Ministério da Saúde, Secretaria de Vigilância em Saúde, Departamento de Vigilância, Prevenção e Controle das Infecções Sexualmente Transmissíveis, do HIV/Aids e das Hepatites Virais; 2019.
- Desta A, Biru TT, Kefale AT. Health related quality of life of people receiving highly active antiretroviral therapy in Southwest Ethiopia. PLoS One 2020;15(8):e0237013. DOI: 10.1371/journal.pone.0237013
- Ndlovu SS, Ghazi T, Chuturgoon AA. The Potential of Moringa oleifera to Ameliorate HAART-Induced Pathophysiological Complications. Cells 2022;24;11(19):2981. DOI: 10.3390/cells11192981
- Achila OO, Abrhaley F, Kesete Y, Tesfaldet F, Alazar F, Fisshaye L, et al. Dyslipidemia and associated risk factors among HIV/AIDS patients on HAART in Asmara, Eritrea. PLoS One 2022:1;17(7):e0270838. DOI: 10.1371/journal.pone.0270838
- Abreu JM, Nogueira ABB, Villela MM, Módolo DM, Panaro TC, Setubal S, et al. Low bone mass and vitamin D in Brazilian people living with HIV under antiretroviral therapy. Arch Osteoporos 2022;17(1):40. DOI: 10.1007/s11657-022-01088-8
- Mumena CH, Mudhihiri MH, Sasi R, Mlawa M, Nyerembe S, Akimbekov NS, et al. The relevance of vitamin D in the oral health of HIV infected patients. J Steroid Biochem Mol Biol 2021;211:105905. DOI: 10.1016/j.jsbmb.2021.105905
- 10. Walsh J S, Bowles S, Evans AL. Vitamin D in obesity. Curr Opin Endocrinol Diabetes Obes 2017;24(6):389-94. DOI: 10.1097/MED.000000000000371
- Alvarez N, Jimenez W, Rugeles MT. The Potential Protective Role of Vitamin D Supplementation on HIV-1 Infection. Front Immunol 2019;10:1-12. DOI: 10.3389/ fimmu.2019.02291
- Da Cunha CT, Silva Pereira DE, do Nascimento CX, Oliveira Tomiya MT, de Sousa BS, de Medeiros BO, et al. Níveis séricos de vitamina D em pacientes portadores de HIV e sua associação com fatores clínicos e nutricionais. Nutrición Clínica y Dietética Hospitalaria 2019;39(2):140-7.
- WHO. World Health Organization. Physical Status: the use and interpretation of anthropometry. Genebra: WHO; 1995 (WHO Technical Report Series, n. 854).
- WHO. World Health Organization. Appropriate body-mass index for Asian populations and its implications for policy and intervention strategies. Lancet (London, England); 2004;363(9403):157. DOI: 10.1016/S0140-6736(03)15268-3
- Corrêa MM, Facchini LA, Thumé E, Oliveira ERAD, Tomasi E. Habilidade da razão cintura-estatura na identificação de risco à saúde. Revista de Saúde Pública 2019;53:66. DOI: 10.11606/s1518-8787.2019053000895
- Valdez R. A simple model-based index of abdominal adiposity. J Clin Epidemiol 1991;44(9):955-6. DOI: 10.1016/0895-4356(91)90059-I
- Ashwell M, Hsieh SD. Six reasons why the waist-to-height ratio is a rapid and effective global indicator for health risks of obesity and how its use could simplify the international public health message on obesity. Int J Food Sci Nut 2005;56(5):303-7.
- Pitanga FJG, Lessa I. Associação entre indicadores antropométricos de obesidade e risco coronariano em adultos na cidade de Salvador, Bahia, Brasil. Revista Brasileira de Epidemiologia 2007;10:239-48. DOI: 10.1590/S1415-790X2007000200011
- Tarastchuk JCE, Guérios ÊE, Bueno RDRL, Andrade PMPD, Nercolini DC, Ferraz JGG, et al. Obesity and coronary intervention: should we con- tinue to use Body Mass Index as a risk factor? Arquivos Brasileiros de Cardiologia 2008;90(5):311-6.
- Lohman TG, Roche AF, Martorell R. Anthropometric standardization reference manual. Champaign, Illinois, Human Kinetics, Inc.; 1988.
- Neyestani TR, Gharavi A, Kalayi A. Determination of serum 25-hydroxycholecalciferol using highperformance liquid cromatography: a reliable tool for assessment of vitamin D status. Int J Vitam Nutr Res 2007;77(5):341-6.
- 22. Ferreira CDS, Maeda SS, Batista MC, Lazaretti-Castro M, Vasconcellos LDS, Madeira M, et al. Posicionamento Oficial da Sociedade Brasileira de Patologia Clínica/Medicina Laboratorial (SBPC/ML) e da Sociedade Brasileira de Endocrinologia e Metabologia (SBEM)–Intervalos de Referência da Vitamina D-25 (OH) D. Sociedade Brasileira de Patologia Clínica. J Bras Patol Med Lab 2018;53(6):377-81.
- 23. Stata Corporation. Guia do usuário do Stata: versão 13. Stata Press; 2001
- 24. Kimball S, Fuleihan Gel-H, Vieth R. Vitamin D: a growing perspective. Crit Rev Clin Lab Sci 2008;45(4):339-414. DOI: 10.1080/10408360802165295
- Raymond-Lezman JR, Riskin SI. Benefits and Risks of Sun Exposure to Maintain Adequate Vitamin D Levels. Cureus 2023;5;15(5):e38578. DOI: 10.7759/ cureus.38578

- Nguyen HS, Van Tran K, Chen SY, Tam KW. A Systematic Review and Meta-Analysis of Randomized Controlled Trials of the Effects of Vitamin D Supplementation on Children and Young Adults with HIV Infection. J Nutr 2023;153(1):138-47. DOI: 10.1016/j.tjnut.2022.10.008
- Lerner AM, Eisinger RW, Fauci AS. Comorbidities in Persons With HIV: The Lingering Challenge. JAMA. 2020;323(1):19-20. DOI: 10.1001/jama.2019.19775
- Beard JA, Bearden A, Striker R. Vitamina D e o estado antiviral. Journal of Clinical Virology: a publicação oficial da Pan American Society for Clinical Virology 2011;50(3):194- 200. DOI: 10.1016/j.jcv.2010.12.006
- Institute of Medicine (US) Committee to Review Dietary Reference Intakes for Vitamin D and Calcium; Ross AC, Taylor CL, Yaktine AL, et al., editors. Dietary Reference Intakes for Calcium and Vitamin D. Washington (DC): National Academies Press (US); 2011. 7, Dietary Intake Assessment. Available from: https:// www.ncbi.nlm.nih.gov/books/NBK56075/
- Golden, NH, Abrams, SA, Comitê de Nutrição, Daniels, SR, Abrams, SA, Corkins, MR, et al. Optimizing Bone Health in Children and Adolescents. Pediatrics October 2014;134(4):e1229-e1243. DOI: 10.1542/peds.2014-2173
- Gautam N, Dayal R, Agarwal D, Kumar R, Singh TP, Hussain T, et al. Role of Multivitamins, Micronutrients and Probiotics Supplementation in Management of HIV Infected Children. The Indian Journal of Pediatrics 2014;81:1315-20. DOI: 10.1007/s12098-014-1407-6
- 3Shepherd L, Souberbielle JC, Bastard JP, Fellahi S, Capeau J, Reekie J, et al. Prognostic value of vitamin D level for all-cause mortality, and association with inflammatory markers, in HIV infected persons. J Infect Dis 2014;210(2):234-43.
- Duarte C, Carvalheiro H, Rodrigues AM, Dias SS, Marques A, Santiago T, et al. Prevalence of vitamin D deficiency and its predictors in the Portuguese population: a nationwide population-based study. Arch Osteoporos 2020;15(1):36. DOI: 10.1007/s11657-020-0695-x. Erratum in: Arch Osteoporos 2020;15(1):55. DOI: 10.1007/s11657-020-00728-1
- Ghosh A, S M, Sunny AS, Diwakar L, Issac TG. Prevalence and patterns of vitamin D deficiency and its role in cognitive functioning in a cohort from South India. Sci Rep 2024;14(1):11215. DOI: 10.1038/s41598-024-62010-5
- Mendes MM, Gomes APO, Araújo MM, Coelho ASG, Carvalho KMB, Botelho PB. Prevalence of vitamin D deficiency in South America: a systematic review and meta-analysis. Nutr Rev 2023;81(10):1290-309. DOI: 10.1093/nutrit/nuad010
- Siddiqee MH, Bhattacharjee B, Siddiqi UR, MeshbahurRahman M. High prevalence of vitamin D deficiency among the South Asian adults: a systematic review and meta-analysis. BMC Public Health 2021;21(1):1823. DOI: 10.1186/s12889-021-11888-1
- Janus SE, Durieux JC, Hajjari J, Carneiro H, McComsey GA. Inflammation-mediated vitamin K and vitamin D effects on vascular calcifications in people with HIV on active antiretroviral therapy. AIDS 2022;36(5):647-55. DOI: 10.1097/ QAD.00000000003149
- Lee S, Lee JE, Lee SO, Sim YK, Lee SH. Influence of Vitamin D Deficiency on the Development of Opportunistic Infection in People Living with HIV/AIDS (PWHAs). J Am Coll Nutr 2021;40(6):545-50. DOI: 10.1080/07315724.2020.1805043
- Canuto JMP, Canuto VMP, Lima MHAD, Omena ALCSD, Morais TMDL, Paiva AM, et al. Risk factors associated with hypovitaminosis D in HIV/Aids-infected adults. Archives of Endocrinology and Metabolism 2015;59(1):34-41. DOI: 10.1590/2359-3997000000007
- Eisinger RW, Fauci AS. Ending the HIV/AIDS pandemic. Emerging Infectious Diseases 2018;24(3):413. DOI: 10.3201/eid2403.171797
- Lundgren JD, Borges AH, Neaton JD. Serious Non-AIDS Conditions in HIV: Benefitof Early ART. Current HIV/AIDS Reports 2018;15(2):162-71. DOI: 10.1007/ s11904-018-0387-y
- Hamill MM, Ward KA, Pettifor J, Norris SA, Prentice A. Bone mass, body composition and vitamin D status of ARV-naïve, urban, black South African women with HIV infection, stratified by CD 4 count. Osteoporosis International 2013;24(11):2855-61. DOI: 10.1007/s00198-013-2373-y
- Brown, Todd T. Recomendações para avaliação e tratamento de doenças ósseas no HIV. Doenças Infecciosas Clínicas 2015;60(8):1242-51.
- Hamill MM, Pettifor JM, Ward KA, Norris SA, Prentice A. Bone mineral density, body composition, and mineral homeostasis over 24 months in urban South African women with HIV exposed to antiretroviral therapy. JBMR Plus 2020;4(5):e10343. DOI: 10.1002/jbm4.10343
- 45. Gebremichael DY, Hadush KT, Kebede EM, Zegeye RT. Food Insecurity, Nutritional Status, and Factors Associated with Malnutrition among People Living with HIV/AIDS Attending Antiretroviral Therapy at Public Health Facilities in West Shewa Zone, Central Ethiopia. Biomed Res Int 2018. DOI: 10.1155/2018/1913534