

Brief Communication: Frailty and Neurocognitive Impairment in Older People Living with HIV: A Cross-Sectional Study from Southeastern Brazil

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Short Report

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Abstract

Background: Frailty and HIV-associated neurocognitive disorders are common but underrecognized in aging people living with HIV (PLWH)

Methods: We conducted a cross-sectional study of 128 PLWH aged ≥ 50 years, using the Fried Frailty Phenotype and the International HIV Dementia Scale (IHDS).

Results: Mean age was 59.6 years, and 57.8% were male. Frailty status, including 8.6% frail and 52.3% pre-frail, was associated with lower BMI ($p = 0.035$). Positive neurocognitive screening (57.8%) was associated with lower education, polypharmacy, and falls (32.4% vs. 13.0%; $p = 0.011$).

Conclusions: Frailty and cognitive impairment are prevalent among aging PLWH; falls were significantly associated with positive neurocognitive screening.

Introduction

Advances in antiretroviral therapy (ART) have substantially increased life expectancy among people living with HIV (PLWH), resulting in a growing population of older adults exposed to age-related conditions^{1–3}. Among these, frailty and HIV-associated neurocognitive disorders (HAND) are particularly relevant because of their impact on morbidity, functional decline, and quality of life^{1–11}

Despite international recommendations for routine screening¹², there is no consensus on the optimal instruments, and their implementation in clinical practice remains limited, particularly in middle-income settings¹. This study aimed to determine the prevalence of frailty and positive screening for neurocognitive impairment among PLWH aged 50 years or older and to identify associated factors.

Methods

This cross-sectional observational study included 128 PLWH aged ≥ 50 years receiving antiretroviral therapy at a referral center for infectious diseases in southeastern Brazil. Sociodemographic, clinical, and behavioral data were collected, including educational attainment, body mass index (BMI), polypharmacy (defined as concurrent use of ≥ 5 medications), and history of falls in the previous six months. BMI was categorized as < 22 , $22–27$, and > 27 kg/m², following geriatric cut-offs. HIV-related variables, including viral load and CD4 + count, were obtained from electronic medical records.

Frailty was assessed using the Fried Frailty Phenotype¹³, based on five components (unintentional weight loss, self-reported exhaustion, reduced grip strength, slow gait speed, and low physical activity), and participants were classified as non-frail, pre-frail, or frail. Cognitive screening was performed using the International HIV Dementia Scale (IHDS)¹⁴ with scores ≤ 10 defined as positive screening for neurocognitive impairment; this cut-off was chosen for its established feasibility in routine clinical settings. As the IHDS is a screening instrument rather than a diagnostic tool, participants classified as

having a positive screening result are referred to throughout this manuscript as having “positive screening for neurocognitive impairment,” rather than a diagnosis of dementia or HAND.

Statistical analysis

Continuous variables were summarized as means and standard deviations, or medians and ranges, as appropriate, and categorical variables as frequencies and percentages. Normality of continuous variables was assessed using the Shapiro–Wilk test. Group comparisons were performed using Student's t-test or one-way analysis of variance (ANOVA) for continuous variables, and the chi-square test for categorical variables. A two-sided p-value < 0.05 was considered statistically significant. All analyses were performed using SAS software, version 9.4 (SAS Institute, Cary, NC, USA).

Results

A total of 128 participants were included, with a mean age of 59.6 years; 57.8% were male, and most self-identified as white (57.8%) or pardo (33.6%). Most participants (57.8%) had eight years of education or less, and half (50.8%) were classified as overweight (BMI > 27 kg/m²). Polypharmacy was present in 28.1% of participants, and 24.5% reported at least one fall in the previous six months. Virological suppression (viral load < 50 copies/mL) was documented in 85.9% of participants. Full sociodemographic and clinical characteristics are presented in Table 1.

Frailty

Frailty status was classified as non-frail in 39.1%, pre-frail in 52.3%, and frail in 8.6% of participants (Table 2). Reduced muscle strength and low physical activity were the most frequently observed frailty components. In bivariate analysis, lower BMI was the only variable significantly associated with frailty status among the sociodemographic and clinical variables assessed ($p = 0.035$). The proportion of participants classified as frail was 26.7% among those with low BMI (< 22 kg/m²), 2.1% among those with BMI between 22 and 27 kg/m², and 9.2% among those with BMI > 27 kg/m² (Table 2).

Positive screening for neurocognitive impairment

Positive screening for neurocognitive impairment (IHDS ≤ 10) was identified in 74 of 128 participants (57.8%). In bivariate analysis, positive screening was significantly associated with lower educational attainment ($p = 0.003$), polypharmacy ($p = 0.039$), and a history of falls in the previous six months ($p = 0.011$) (Table 2).

Among participants with positive neurocognitive screening, 70.3% had the lowest level of educational attainment, 21.6% had intermediate educational attainment, and only 8.1% had the highest educational level (Table 2). Polypharmacy was more frequent among participants with positive screening than among those without (35.1% vs. 18.5%; Table 2). Similarly, a history of falls in the previous six months

was reported by 31 participants (24.2%) and was more frequent among those with positive neurocognitive screening than among those with IHDS > 10 (32.4% vs. 13.0%, respectively; $p = 0.011$; Table 2).

Table 1
Sociodemographic, clinical, and functional characteristics of the study population
(N = 128)

Variable	Category	n	%
HIV viral load	Undetectable (< 50 copies/mL)	110	85.9
	Detectable ($\geq$ 50 copies/mL)	18	14.1
CD4 + count (cells/mm ³)	> 500	93	72.7
	350–500	18	14.1
	200–350	12	9.4
	< 200	5	3.9
Age group (years)	50–59	77	60.2
	60–69	42	32.8
	$\geq$ 70	9	7.0
Sex at birth	Female	54	42.2
	Male	74	57.8
Race/skin color (self-reported)	White	74	57.8
	Pardo*	43	33.6
	Black	9	7.0
	Indigenous	2	1.6
Educational level	$\leq$ 8 years	74	57.8
	9–11 years	37	28.9
	> 11 years	17	13.3
BMI category (kg/m ²)	< 22 (low body mass)	15	11.7
	22–27 (eutrophic)	48	37.5
	> 27 (overweight)	65	50.8
Polypharmacy	No	92	71.9
	Yes	36	28.1
Falls (last 6 months)	No	97	75.5
	Yes	31	24.5

**Pardo is a Brazilian census category defined by the Brazilian Institute of Geography and Statistics (IBGE), referring to individuals of mixed ancestry. BMI categories followed geriatric cut-offs. Polypharmacy was defined as the use of ≥ 5 medications.*

Table 2
Bivariate associations between selected variables and positive neurocognitive screening or frailty (N = 128)

Variable	Category	IHDS > 10 (no risk) n (%)	IHDS $\leq$ 10 (risk) n (%)	p-value
Frailty status	Non-frail	23 (42.6)	27 (36.5)	0.067
	Pre-frail	30 (55.6)	37 (50.0)	
	Frail	1 (1.9)	10 (13.5)	
Educational level	≤ 8 years	22 (40.7)	52 (70.3)	0.003
	9–11 years	21 (38.9)	16 (21.6)	
	> 11 years	11 (20.4)	6 (8.1)	
Polypharmacy	No	44 (81.5)	48 (64.9)	0.039
	Yes	10 (18.5)	26 (35.1)	
Falls (last 6 months)	No	47 (87.0)	50 (67.6)	0.011
	Yes	7 (13.0)	24 (32.4)	
Total		54	74	
Frailty by BMI category (Category Total n Frail n (%) p-value)				
	< 22 (low)	15	4 (26.7)	0.035
	22–27 (normal)	48	1 (2.1)	
	> 27 (overweight)	65	6 (9.2)	
	Total	128	11 (8.6)	

Associations were assessed using the chi-square test.

Discussion

In this cross-sectional study of older PLWH receiving care at a referral center in southeastern Brazil, we observed a high prevalence of pre-frailty and positive screening for neurocognitive impairment, despite high rates of virological suppression. These findings are consistent with previous reports and reinforce the importance of incorporating geriatric assessment into routine HIV care, even among patients with well-controlled infection^{2,4,15–17}. A recent systematic review of risk factors for HIV-associated

neurocognitive impairment and frailty among aging PLWH in Latin America similarly highlighted the high burden of these conditions across the region and the persistent gaps in their systematic screening in clinical practice¹⁸.

Frailty was associated with lower BMI, suggesting a possible contribution of sarcopenia, although this was not directly measured in our study. This finding is consistent with previous studies linking frailty to reduced muscle strength and physical inactivity in PLWH^{4,17}. Given the cross-sectional design of our study, this association should be interpreted as correlational rather than causal; longitudinal studies are needed to clarify the temporal relationship between body composition and the development of frailty in this population. Nonetheless, the predominance of reduced strength and low physical activity among frailty components in our cohort supports the potential relevance of modifiable determinants, and interventions focused on resistance exercise, physical rehabilitation, and nutritional support may be beneficial^{4,17}.

Positive screening for neurocognitive impairment (IHDS ≤ 10) was identified in 57.8% of participants, a prevalence consistent with previous studies reporting high rates of positive screening even among individuals without overt cognitive complaints^{2,16}. The observed association between lower educational attainment and a positive screening result may reflect, at least in part, the influence of education on cognitive test performance and cognitive reserve, rather than a direct effect on underlying neurocognitive function; this should be considered when interpreting IHDS results in populations with heterogeneous educational backgrounds.

Polypharmacy was also associated with positive neurocognitive screening in our cohort, in line with recent evidence linking polypharmacy to adverse functional outcomes, including slower gait speed and recurrent falls, among older people with HIV¹⁹. The history of falls in the previous six months was significantly more frequent among participants with positive neurocognitive screening (32.4% vs. 13.0%; $p = 0.011$), suggesting that falls may serve as a clinically useful marker of neurocognitive risk in aging PLWH, warranting further investigation in longitudinal cohorts.

Although not statistically significant, we also observed a numerical trend toward a higher proportion of frailty among participants with positive neurocognitive screening: only 1.9% of participants without cognitive risk (IHDS > 10) were classified as frail, compared with 13.5% of those with positive screening (IHDS ≤ 10) ($p = 0.067$). While this association did not reach conventional statistical significance, possibly due to limited power in the frail subgroup ($n = 11$), it is consistent with the broader literature suggesting a link between frailty and neurocognitive impairment in aging PLWH, as previously reported in cohorts of older adults with symptomatic cognitive impairment², and warrants further investigation in larger, longitudinal cohorts.

Our findings should be interpreted in the context of the broader literature on aging with HIV. Similar to cohorts described in other Brazilian and Latin American settings, frailty and positive neurocognitive screening were common despite favorable virological control, underscoring that immunovirological

success does not preclude the development of geriatric syndromes in this population¹⁸. Efforts to refine screening tools for use in socioeconomically and educationally diverse populations, such as the recently proposed revised Veterans Aging Cohort Study index, may improve the discrimination of neurocognitive impairment and frailty in future studies.

Declarations

Ethics approval statement

This study was approved by the local Research Ethics Committee (CAAE: 79137824.8.0000.5411). All procedures were conducted in accordance with the Declaration of Helsinki.

Patient consent statement

Written informed consent was obtained from all participants.

Data availability statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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Conflict of interest disclosure

The authors declare no conflicts of interest.

Clinical trial registration

Not applicable.

Permission to reproduce material from other sources

Not applicable.

Author Contribution

JOR contributed to data collection, statistical analysis, and writing of the original manuscript. TLS contributed to data collection. LRS contributed to study supervision and critical review of the manuscript. All authors read and approved the final manuscript.

References

1. Kehler DS, Milic J, Guaraldi G, Fulop T, Falutz J. Frailty in older people living with HIV: current status and clinical management. *BMC Geriatr.* 2022;22(1):919.
2. Hosaka KRJ, Greene M, Premeaux TA, et al. Geriatric Syndromes in Older Adults Living with HIV and Cognitive Impairment. *J Am Geriatr Soc.* 2019;67(9):1913–6.
3. Sanmarti M, Ibáñez L, Huertas S, et al. HIV-associated neurocognitive disorders. *J Mol Psychiatry.* 2014;2(1):2.
4. Erlandson KM, Piggott DA, Frailty. Moving from Characterization to Intervention. *Curr HIV/AIDS Rep.* 2021;18(3):157–75.
5. Guaraldi G, Malagoli A, Theou O, et al. Correlates of frailty phenotype and frailty index and their associations with clinical outcomes. *HIV Med.* 2017;18(10):764–71.
6. McMillan JM, Krentz HB, Gill MJ, Hogan DB. An Emerging Concern-High Rates of Frailty among Middle-aged and Older Individuals Living with HIV. *Can Geriatr J.* 2019;22(4):190–8.
7. Kooij KW, Wit FW, Schouten J, et al. HIV infection is independently associated with frailty in middle-aged HIV type 1-infected individuals compared with similar but uninfected controls. *AIDS.* 2016;30(2):241–50.
8. Petit N, Enel P, Ravaux I, et al. Frail and pre-frail phenotype is associated with pain in older HIV-infected patients. *Med (Baltim).* 2018;97(6):e9852.
9. Horvath S, Levine AJ. HIV-1 Infection Accelerates Age According to the Epigenetic Clock. *J Infect Dis.* 2015;212(10):1563–73.
10. Magaki SD, Vinters HV, Williams CK, et al. Neuropathologic Findings in Elderly HIV-Positive Individuals. *J Neuropathol Exp Neurol.* 2022;81(7):565–76.
11. Rosca EC, Tadger P, Cornea A, Tudor R, Oancea C, Simu M. International HIV Dementia Scale for HIV-Associated Neurocognitive Disorders: A Systematic Review and Meta-Analysis. *Diagnostics (Basel).* 2021;11(6):1124.
12. European AIDS Clinical Society (EACS). EACS Guidelines version 11.0. October 2021. Available at: <https://www.eacsociety.org/guidelines/>
13. Fried LP, Tangen CM, Walston J, et al. Frailty in Older Adults: Evidence for a Phenotype. *J Gerontol Biol Sci Med Sci.* 2001;56(3):M146–56.
14. Sacktor NC, Wong M, Nakasujja N, et al. The International HIV Dementia Scale: a new rapid screening test for HIV dementia. *AIDS.* 2005;19(13):1367–74.
15. Heaton RK, Clifford DB, Franklin DR, et al. HIV-associated neurocognitive disorders persist in the era of potent antiretroviral therapy: CHARTER study. *Neurology.* 2010;75(23):2087–96.
16. Simioni S, Cavassini M, Annoni JM, et al. Cognitive dysfunction in HIV patients despite long-standing suppression of viremia. *AIDS.* 2010;24(9):1243–50.
17. Morante-Ruiz M, Sanabria-Giron PC, Rubio-Martin R, et al. A Perspective on Frailty and its Predisposing Factors among People Living with HIV. *Curr HIV Res.* 2024;22(6):349–53.

18. Diaz MM, Pokala SS, Saavedra Forero LM, et al. Risk factors for HIV-associated neurocognitive impairment and frailty in aging people with HIV in Latin America: a systematic review. *BMC Neurol.* 2026;26. 10.1186/s12883-026-04767-y.
19. Kosana P, Wu K, Tassiopoulos K, Letendre S, Ma Q, Paul R, et al. Polypharmacy is associated with slow gait speed and recurrent falls in older people with HIV. *Clin Infect Dis.* 2024;78(11):1608–16.