


Prevalence of Frailty Phenotypes in Older People Living with HIV: A Cross-Sectional Study from Brazil

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Abstract

Background: Frailty may affect people living with HIV (PLHIV) prematurely. Fried's frailty phenotype, composed of 5 criteria, is one of the most used instruments for its assessment. This study aimed to determine the prevalence of these criteria among PLHIV classified as prefrail and frail in Brazil.

Methods: A cross-sectional study analyzed the prevalence of the Frailty Phenotype in Brazil with 670 individuals aged ≥ 50 years and undetectable viral load.

Results: The prevalence of prefrail and frail individuals was 50.7% and 13.6%, respectively. A low level of physical activity was the most prevalent criterion (50.9%). Except for unintentional weight loss, all other criteria were more prevalent among individuals with lower education levels. All criteria were more prevalent among individuals of lower socioeconomic status than among those of moderate or high status ($P < .05$).

Conclusions: A low level of physical activity was the component that most contributed to PLHIV being considered prefrail or frail.

Keywords

HIV, aging, physical activity, frailty, frailty phenotype criteria

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Introduction

Frailty is a multisystemic condition often associated with aging, in which there is a decline in an individual's physical and functional reserve, leaving them vulnerable to stressful events¹ and associated with a higher risk of serious health outcomes, such as falls, hospitalizations, disability, and death.¹ People living with HIV (PLHIV) may be prematurely affected by frailty when compared to individuals in the general population.²

Several instruments in the literature assess frailty, however, Fried's frailty phenotype³ is the most widely used, both in research with the general population and in PLHIV.^{4,5} In this instrument, individuals are evaluated according to the presence of 5 criteria: unintentional weight loss, self-reported exhaustion, slow gait, weakness, and low level of physical activity. The score obtained in each criterion results in the classification of individuals into three distinct groups: frail, prefrail, or robust.³

In a recent review of 26 studies that used Fried's phenotype,³ the combined prevalence of frailty and prefrailty among PLHIV aged ≥ 50 years was 10.9% (8.1%-14.2%) and 47.2% (40.1%-54.4%), respectively.⁶ However, few of these studies discriminate the prevalence of each of the 5 criteria that constitute the frailty phenotype.

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Knowing the individual contribution of these criteria is important due to the dynamic nature of frailty.¹ The transition from a state of robustness or prefrailty to frailty can be prevented or delayed by adopting measures targeted to specific components of the frailty phenotype.⁷ The objective of this study was to determine the prevalence of each of these components among PLHIV classified as prefrail and frail attended in specialized HIV/AIDS services in Brazil.

Methods

Study Design and Population

A cross-sectional study was conducted with PLHIV attended in the only two public services specialized in outpatient care for HIV/AIDS in a large municipality of Brazil. The study was conducted in 2 time periods, due to the COVID-19 pandemic: from November 2019 to March 2020 and from September 2020 to November 2021 and included all PLHIV aged ≥ 50 years, using antiretroviral therapy (ART), and with undetectable viral load from the 2 services. Individuals with active neoplasms, severe cognitive or psychiatric disorders, wheelchair users, and bedridden individuals were excluded from the study.

Data Collection

Participants were interviewed to obtain sociodemographic, behavioral, and clinical data and underwent a physical assessment to measure weight, height, body mass index (BMI), and dental condition. Medical records were reviewed to verify comorbidities and history of antiretroviral use. CD4 and CD8 cell count and viral load were obtained from the national database.

The frailty phenotype was evaluated using the criteria suggested by Fried et al.³ Individuals with no positive criteria were classified as robust, those with 1 or 2 positive criteria were classified as prefrail, and those with 3 or more positive criteria were classified as frail.³ Weight loss was defined as the unintentional loss of ≥ 4.5 kg or $\geq 5\%$ of body weight compared to the measurement recorded in the medical record in the last year. Two questions (No. 7 and No. 20) from the International Depression Questionnaire⁸ were used to evaluate self-reported exhaustion. Weakness, adjusted for sex and BMI, was evaluated by the mean obtained from three values of grip strength (kg) of the dominant hand using a Saehan[®] dynamometer. Gait speed was evaluated by timing the seconds taken to walk the distance of 4.6 meters, adjusting the results for sex and height. Low level of physical activity was assessed through self-reported weekly caloric expenditure stratified by sex using the Minnesota Leisure-Time Physical Activity Questionnaire.⁹ The cutoff points used for muscle strength, gait speed, and physical activity were those previously determined by Fried et al.³

The sociodemographic and behavioral variables included sex, age, education level, economic class, smoking, alcohol consumption, and illicit drug use. The following comorbidities were evaluated: depression, diabetes, dyslipidemia, cardiovascular diseases,

thyroid disease, chronic pain, chronic obstructive pulmonary disease, chronic kidney disease, and systemic arterial hypertension. Multimorbidity¹⁰ was defined as the presence of two or more of the abovementioned comorbidities, except depression. Polypharmacy was defined as the use of five or more medications, except for ART.¹¹

Functional dentition was defined as ≤ 20 teeth present.¹² Cognitive capacity was assessed through questions that addressed subjective complaints of cognitive decline¹³ and by the Mini-Mental State Examination (MMSE).¹⁴ Participants in the study were also evaluated for a history of falls (≥ 2 falls) and hospitalizations in the last 12 months.

Parameters related to HIV included time of diagnosis, CD4, and CD8 cell counts, and CD4/CD8 ratio. Regarding ART, the duration of use, history of treatment adherence, and the number of ART regimens used were evaluated.

Statistical Analysis

Initially, the study population was characterized according to sociodemographic, lifestyle, health, and HIV-related variables in total and concerning each of the 5 criteria of the frailty phenotype. The association with each criterion was tested for categorical variables using the chi-square test and for quantitative variables using the nonparametric Mann–Whitney test.

In sequence, the prevalence of prefrailty and frailty for the total study population was determined, and the prevalence of each criterion was calculated among prefrail and frail individuals and stratified by sex, age group (< 60 and ≥ 60 years), educational level (low and moderate/high), and socioeconomic status (low and moderate/high), using the chi-square test to detect differences in the proportion of individuals who met the criterion in each subgroup.

Finally, radial graphs were used to represent the frequency of each criterion among prefrail and frail individuals according to sex and age group. The significance level adopted for all tests was 5%. All analyses were performed using the IBM SPSS Statistics 28.0 computer program.

Ethical Approval, Informed Consent, and Registration

The study was approved by the Human Research Ethics Committee, no. 3.558.689. Written consent was obtained from all participants. As an observational cohort, this study was not registered, and the study protocol has not been previously published.

Results

From the 670 individuals who participated in this study, 239 (35.7%) did not score in any of the criteria and were considered robust, 340 (50.7%) scored in 1 or 2 criteria and were classified as prefrail, and 91 (13.6%) scored in 3 or more criteria and were considered frail.

Overall, a low level of physical activity (50.9%) was the most prevalent criterion, followed by self-reported exhaustion (28.1%), weakness (24.0%), weight loss (6.6%), and slow gait (6.3%). A low level of physical activity was present in 98.9% of frail individuals and 73.8% of prefrail individuals. Moreover, among the 206 individuals who scored in only one criterion, a low level of physical activity was also the most prevalent component (66.5%). Among frail individuals, weight loss was the least prevalent criterion (26.4%), and among prefrail individuals, slow gait was the least scored criterion (2.1%) (Figure 1).

The median age was 58 years old, and the majority of participants were male (55.7%). Figure 2 shows the prevalence of each criterion according to sociodemographic variables. Self-reported exhaustion, slow gait, and low levels of physical activity were more prevalent among women than among men ($P < .05$). A higher prevalence of weakness, slow gait, and low level of physical activity was observed among individuals aged 60 years or older compared to those younger ($P < .05$). Except for weight loss, all other criteria were more prevalent among individuals with lower education levels than among those with higher. Regarding economic class, all criteria were more prevalent among individuals from lower economic classes than among those from moderate or high classes ($P < .05$).

Table 1 provides descriptive data on the study population according to each of the 5 criteria investigated. Smokers had a higher prevalence of weight loss, self-reported exhaustion, and muscular weakness than nonsmokers. Frequent alcohol consumption was unrelated to any of the criteria, and illicit drug use was more prevalent among those with self-reported exhaustion.

Although hypertension was the most frequent comorbidity, it was not associated with a higher prevalence of any of the criteria. On the other hand, cardiovascular disease (8.7%) was

associated with all components of the frailty phenotype. Except for weight loss, all other criteria were more prevalent among individuals with multimorbidity and polypharmacy. The absence of functional dentition and the use of dental prostheses were more prevalent among individuals with weakness, slow gait, and low physical activity. All criteria were more prevalent among individuals with subjective cognitive complaints, lower scores on the MMSE, those who had fallen, and those who had been hospitalized in the last year (Table 1).

A higher prevalence of muscular weakness and low level of physical activity was observed among individuals diagnosed with HIV aged 50 years or older. Among those with a history of low adherence to ART, a higher prevalence of slow gait and low levels of physical activity was observed (Table 1).

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Figures 3 and 4 demonstrate the prevalence of criteria by sex and age, respectively. Low levels of physical activity and self-reported exhaustion were the most prevalent criteria in frail individuals of both sexes and age groups. Muscular weakness was the criterion that most contributed to differentiating frail men from frail women. Regarding prefrailty, the prevalence of criteria was similar for both sexes (Figure 3). Slow gait was the criterion that most contributed to differentiating frail individuals aged ≥ 60 years from those aged < 60 years. On the other hand, among prefrail individuals, the prevalence of criteria was similar for both age groups (Figure 4).

Discussion

The present epidemiological study identified, in a large sample of PLHIV, a prevalence of prefrailty of 50.7% and frailty of 13.6%. When analyzing the individual prevalence of the criteria

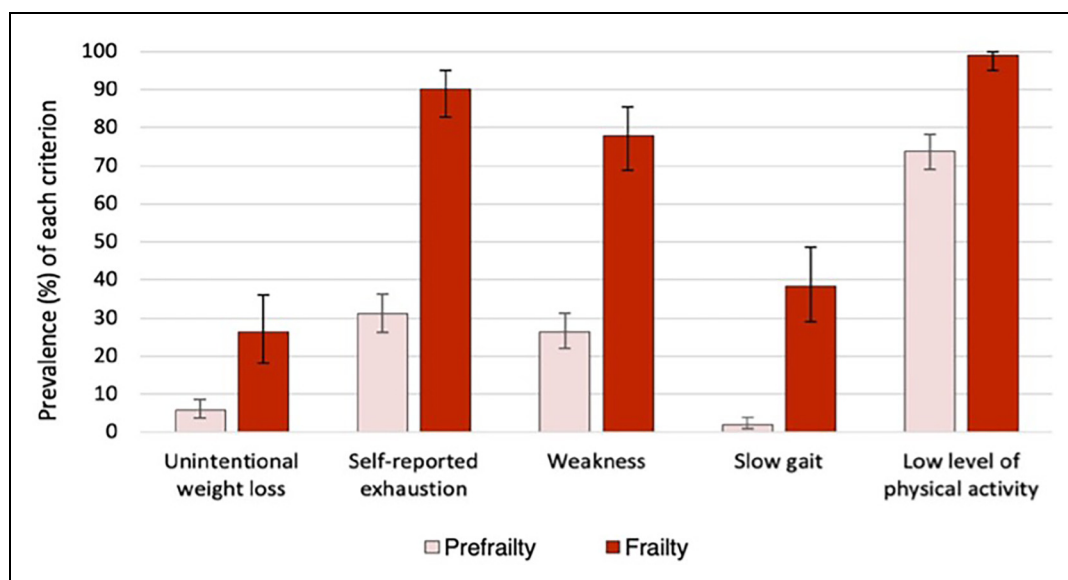


Figure 1. Prevalence of each frailty phenotype criterion.

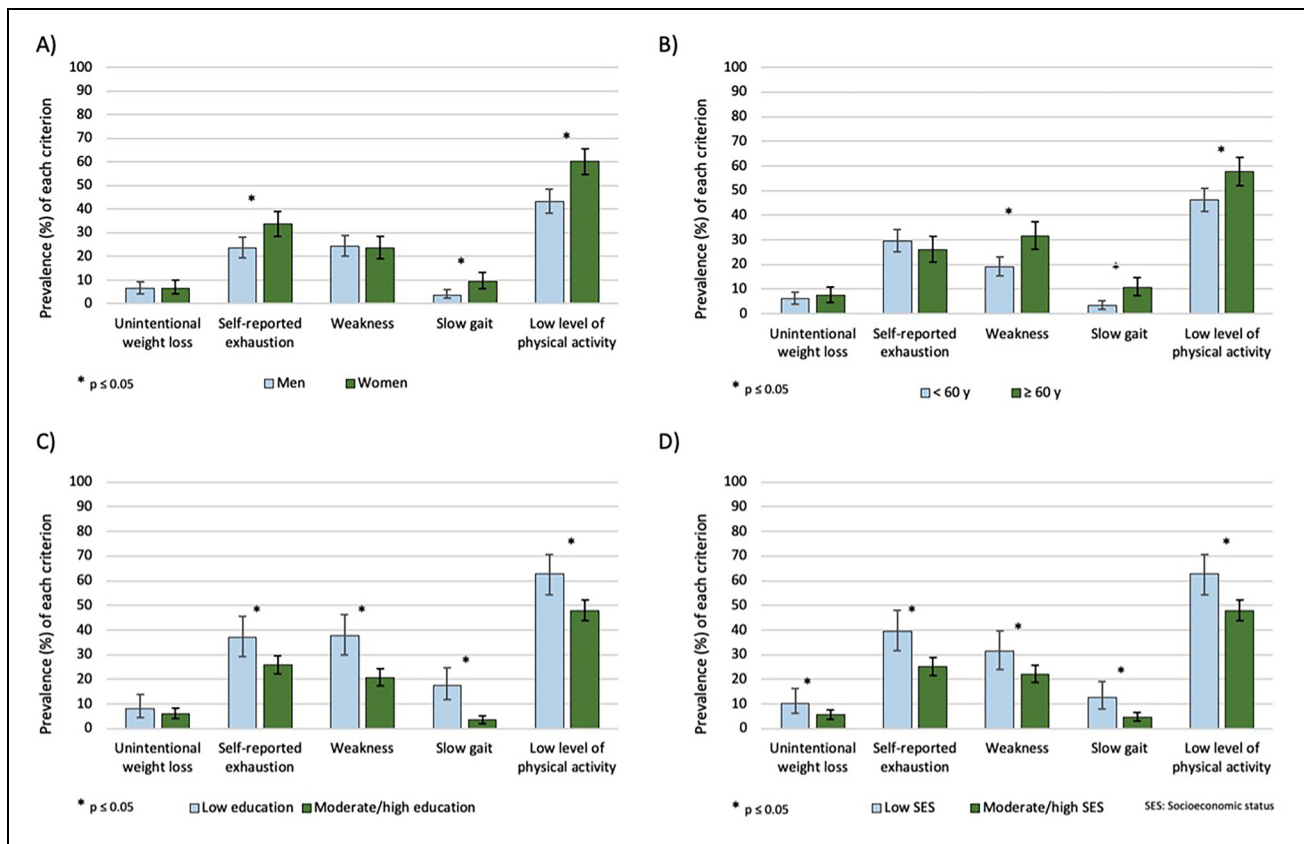


Figure 2. Prevalence of each frailty phenotype criterion by sociodemographic variables.

considered for this classification, a low level of physical activity was the most prevalent component, being observed in over half of the surveyed individuals (50.9%), followed by self-reported exhaustion (28.1%) and weakness (24.0%). Unintentional weight loss (6.6%) and slow gait (6.3%) were the least prevalent criteria. The low level of physical activity criterion had the highest number of associations with the researched variables, while unintentional weight loss had the lowest number.

An individual analysis of the criteria demonstrates that they vary in their frequency of distribution and present different associations with various risk factors and adverse events such as falls, hospitalizations, and death.^{1,4,15-17} Furthermore, there seems to be an order to the appearance of the criteria during the progression to frailty, starting with weakness, slow gait, and low level of physical activity and culminating in self-reported exhaustion and unintentional weight loss.¹

According to Fried et al,³ the prevalence of each criterion among individuals in the general North American population aged 65 or older was 22% for low physical activity, 20% for slow gait, 20% for weakness, 17% for self-reported exhaustion, and 6% for unintentional weight loss.³ In Brazil, a survey with people in the general population aged ≥ 50 observed a higher prevalence of self-reported exhaustion (28.6%), weakness (22.6%), slow gait (20.5%), low level of physical activity (19.8%), and unintentional weight loss (7.4%).¹⁸

In previous studies with PLHIV, some reported low levels of physical activity as the most prevalent component,¹⁹⁻²⁴ others

reported exhaustion,^{16,25,26} and others reported weakness.²⁷⁻³⁰ Moreover, some studies reported no differences in the prevalence of frailty components between PLHIV and individuals from the general population,^{31,32} while significant differences were reported in others.^{16,29}

However, most frailty research uses adapted or modified versions of the frailty phenotype,^{6,33} often changing the way each criterion is measured and, as a result, altering their prevalence and making data comparisons between studies more difficult.³³ Low levels of physical activity and weight loss are the criteria that undergo the most modifications.³³ In fact, Ziller et al³⁴ found that, between 5 different tools to assess physical activity, the prevalence of frailty in the same population ranged from 14.9% to 31.9%.

In this study, physical activity was evaluated as originally proposed by Fried et al,³ through the Minnesota Leisure-Time Physical Activity Questionnaire.⁹ However some authors question its applicability for assessing physical activity in older adults, since it was originally designed to evaluate young, healthy, male individuals,³³ the low level of physical activity found in this study was higher than that reported in previous studies with a similar population,²⁴ and support previous data showing that the level of sedentary behavior among PLHIV is high³⁵ and greater among women than men.³⁶

Self-reported exhaustion or fatigue is a common symptom in PLHIV, even among those on ART with good disease control,³⁷ and is often associated with anxiety and depression.³⁸ As a self-

Table 1. Characteristics of the Study Population According to the Frailty Phenotype Criteria.

Characteristics	Total	Unintentional weight loss	Self-reported exhaustion	Weakness	Slow gait	Low physical activity
Total	670 (100.0)	44 (6.6)	188 (28.1)	161 (24.0)	42 (6.3)	341 (50.9)
Tobacco smoker	175 (26.1)	18 (40.9)*	67 (35.6)**	55 (34.2)*	15 (35.7)	94 (27.6)
Alcoholic beverages drinker	43 (6.4)	3 (6.8)	14 (7.4)	15 (9.3)	2 (4.8)	27 (7.9)
Current illicit drugs user	24 (3.6)	2 (4.5)	12 (6.4)*	4 (2.5)	1 (2.4)	11 (3.2)
Body mass index (kg/m^2), median (IQR)	25.3 (22.5; 28.5)	20.9 (19.2; 24.4)**	25.6 (22.29; 1)	25.4 (21.4; 30)	24.4 (19.7; 30.9)	25.5 (22.4; 29.3)
Multimorbidity (≥ 2 chronic disease)	300 (44.8)	21 (47.7)	106 (56.4)**	93 (57.8)**	30 (71.4)**	185 (54.3)**
Diabetes	123 (18.4)	7 (15.9)	38 (20.2)	43 (26.7)*	11 (26.2)	78 (22.9)*
Dyslipidemia	450 (67.2)	24 (54.5)	128 (68.6)	103 (64.0)	30 (71.4)	246* (72.1)
Cardiovascular disease	58 (8.7)	8 (18.2)*	24 (12.8)*	26 (16.1)**	10 (23.8)**	42 (12.3)**
Hypertension	245 (36.6)	19 (43.2)	79 (42.0)	76 (47.2)*	20 (47.6)	142 (41.6)*
Chronic kidney disease	31 (4.6)	3 (6.8)	11 (5.9)	10 (6.2)	4 (9.5)	19 (5.6)
COPD	14 (2.1)	2 (4.5)	9 (4.8)*	6 (3.7)	3 (7.1)*	8 (2.3)
Chronic pain	76 (11.3)	8 (18.2)	43 (22.9)**	33 (20.5)**	15 (35.7)**	56 (16.4)**
Thyroid disease	51 (7.6)	3 (6.8)	21 (11.2)*	16 (9.9)	6 (14.3)	32 (9.4)
Depression	117 (17.5)	11 (25.0)	66 (33.5)**	35 (21.7)	7 (16.7)	72 (21.1)*
Polypharmacy	76 (11.3)	6 (13.6)	34 (18.1)*	31 (19.3)**	9 (21.4)*	58 (17.0)**
Subjective cognitive complaints	134 (20.0)	20 (45.5)**	80 (42.6)**	47 (29.2)*	14 (33.3)*	90 (26.4)**
MMSE, median (IQR)	28 (26; 29)	26.5 (25; 28)*	27.5 (25; 29)**	27 (24; 28)**	26 (20.8; 28)**	28 (25; 29)**
Use of dental prosthesis	326 (48.7)	23 (52.3)	96 (51.1)	100 (62.1)**	31 (73.8)*	182 (53.4)*
Absence of functional dentition (≤ 20 teeth)	408 (60.9)	31 (70.5)	125 (66.5)	127 (78.9)**	38 (90.5)**	222 (65.1)*
Falls (≥ 2)	43 (6.4)	6 (13.6)*	24 (12.8)**	21 (13.0)**	9 (21.4)**	32 (9.4)*
Hospitalizations	48 (7.2)	9 (20.5)**	25 (13.3)**	27 (16.8)**	9 (21.4)**	36 (10.6)*
Age at diagnosis ≥ 50 Y	230 (34.3)	18 (40.9)	61 (32.4)	74 (46.0)**	22 (52.4)*	130 (38.1)*
Time since HIV diagnosis (Y), median (IQR)	13 (7; 20)	13 (8.3; 23)	14 (7; 20.8)	12 (6; 20)	14 (9.8; 19.3)	13 (9.7; 21)
AIDS history	401 (59.9)	25 (56.8)	108 (57.4)	92 (57.1)	23 (54.8)	201 (58.9)
Current CD4+ cell counts, median (IQR)	627 (453; 819)	652 (506; 890)	646 (458; 820)	590 (430; 790)	588 (411; 792)	645 (451; 820)
CD4+ cell NADIR < 200	381 (56.9)	23 (52.3)	109 (58.0)	94 (58.4)	24 (57.1)	187 (54.8)
CD4+/CD8+ ratio, median (IQR)	0.7 (0.5; 1.0)	0.8 (0.5; 1.1)	0.6 (0.4; 1.0)	0.6 (0.4; 0.9)	0.6 (0.4; 1.1)	0.7 (0.5; 1.0)
Time on art (Y), median (IQR)	10 (6; 17.3)	11.5 (8; 19.3)	11.5 (5; 17)	10 (5; 17.5)	12 (7.3; 16.3)	11 (6; 18.5)
History of low adherence to art	219 (32.7)	12 (27.3)	72 (38.3)	61 (37.9)	20 (47.6)*	128 (37.5)*
Antiretroviral regimens ≥ 5	111 (16.6)	4 (9.1)	29 (15.4)	26 (16.1)	6 (14.3)	62 (18.2)

MMSE, mini-mental state examination; ART, antiretroviral treatment; COPD, chronic obstructive pulmonary disease; IQR, interquartile range.

* $p \leq 0.050$ e ** $p \leq 0.001$.

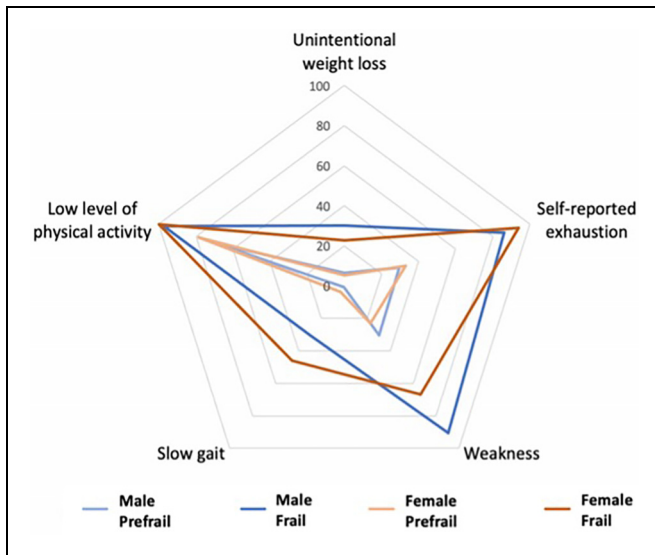


Figure 3. Prevalence of the frailty phenotype criteria according to gender.

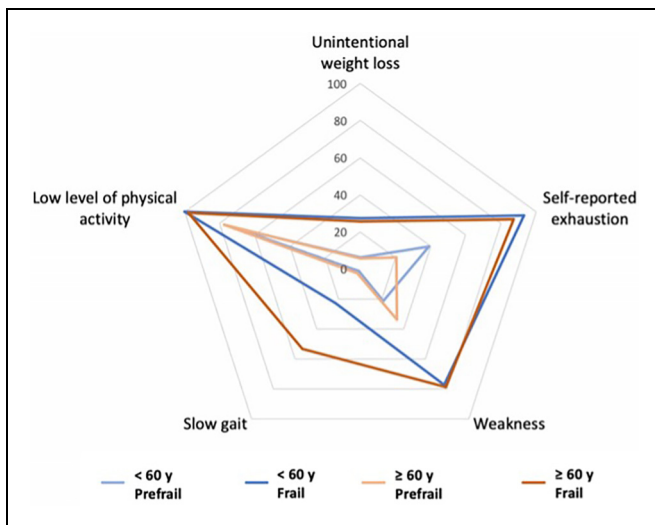


Figure 4. Prevalence of the frailty phenotype criteria according to age group.

reported criterion, its prevalence may be overestimated when including individuals with depressive symptoms.³ However, the exclusion of these individuals from studies that use the frailty phenotype is still a controversial topic.³³ In the study by Koji et al,³² self-reported exhaustion was the most prevalent criterion and the authors observed that depression, although strongly associated with frailty, was not sufficient to explain the higher prevalence of frail and prefrail individuals among PLHIV, compared to the general population. Therefore, in agreement with other authors, this study chose not to exclude individuals with a previous diagnosis of depression.

In the general population, handgrip strength increases until adulthood and begins to decline rapidly from the age of 60, due to changes in body composition, such as loss of muscle

mass and sarcopenia.³⁹ PLHIV has a higher risk of developing this condition.⁴⁰ A previous study showed that men living with HIV, notably those who remained with detectable viral load for a longer time, had a faster decline in handgrip strength after the age of 50 and had about 10 years earlier occurrence of weakness, compared to men of the same age without infection.⁴¹ In addition, the decline in muscle strength and gait speed was also pointed out in a previous study as the factor most associated with frailty among PLHIV.¹⁵ In this study, the criterion of weakness contributed to differentiating frail men from frail women and is consistent with a previous study that demonstrated that the reduction of muscle strength among PLHIV on ART was more evident among men than women.⁴²

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Unintentional weight loss is considered the least informative component among the 5 frailty criteria⁴ and one of the lowest prevalent components in studies with PLHIV.^{26,28,30} In the general older population, unintentional weight loss was the criterion that appeared later, detected a few years before the diagnosis of frailty and related events.¹ Moreover, previously described as one of the main symptoms related to advanced HIV infection, weight loss among PLHIV is now less observed as a result of early treatment. In fact, an increased number of PLHIV on ART are overweight or obese⁴³ corroborating the findings of this study, with more than half of the individuals overweighted or obese.

Slow gait is the main frailty indicator in the general older population and the most predictive phenotype criterion of health-related adverse events.^{4,17} Among PLHIV, the gait speed declines with age and settles earlier and faster than in the general population.⁴⁴ In this study, although it was the least observed criterion, slow gait contributed the most to differentiating older frail individuals from younger frail individuals.

This research showed the association of frailty phenotype criteria with different sociodemographic, behavioral, clinical, and HIV- and ART-related factors. Some of these associations were also observed in previous studies and reinforce the multifactorial nature of frailty⁵ and the need for a broader evaluation of older PLHIV who are in regular use of ART, focusing less on the virus and more on promoting overall health.⁴⁵ Indeed, as observed in this study and previous studies,^{27,30} frailty in PLHIV with good virological control is less related to specific virus-related factors and more associated with factors found in the general population.

One of the main measures to prevent or delay the progression to frailty is to act on sedentarism. Regular physical activity, associated with nutritional supplementation when indicated, has a modifying action on various frailty phenotype criteria and is considered the intervention with the best results.⁷ The data from this study show that women, people aged ≥ 60 years, and those with worse socioeducational conditions should be seen as priority groups for this type of intervention.

In the assessment of cognitive status, each participant was first asked about their perception of their current cognitive ability and then the MMSE test was applied. Both items were significantly associated with prefrail and frail individuals. In a

study by Hsieh et al,⁴⁶ with elderly people from the general population, subjective cognitive decline was a factor independently associated with frailty. The present study, therefore, corroborates this finding also among PLHIV and indicates that evaluation of this variable can be another tool for screening for frailty among PLHIV.

Currently, the health services that provide care to PLHIV need to adapt to the new context provided by the aging of this population.⁴⁵ To meet all the demands resulting from the various potential frailty-related factors, the most appropriate approach is through a multidisciplinary team,⁴⁷ consisting of an infectious disease physician, geriatrician, nursing team, physiotherapist, psychologist, social worker, pharmacist, dentist, among others. Thus, to provide comprehensive care, it is necessary for the health service to provide conditions for the individual to quit smoking and the use of other drugs, encourage the prevention and adequate control of comorbidities, reevaluate the medications in use, and adjust to reduce polypharmacy, and offer evaluation and follow-up of mental and oral health.

The study has some limitations. The COVID-19 pandemic may have influenced some of the results. Despite the research being able to reach 85.6% of those eligible, individuals primarily excluded and those who were not recruited may have reduced their visits to healthcare services precisely because they were more debilitated. Additionally, some of the participants were approached during the local government's measures to contain the viral infection. Such measures, such as travel restrictions and the closure of clubs and gyms, may have favored social isolation, the emergence of depressive symptoms, and a reduction in caloric expenditure among this population, altering the prevalence of some components of the frailty phenotype. An increase in the prevalence of frailty was observed in a recent study conducted with elderly individuals from the general population of European countries that adopted confinement measures to contain the COVID-19 pandemic.⁴⁸

Conclusions

Low levels of physical activity contributed to frailty or prefrailty in PLHIV in this study. Therefore, measures directed toward this criterion, such as promoting regular physical activity and exercise, could improve this population's frailty status, especially for individuals classified as prefrail. Furthermore, the prevalence distribution of the components of the frailty phenotype may vary between men and women living with HIV, and these differences should be considered in approaching this population.

Statements and Declarations

The authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest in the subject matter or materials discussed in this manuscript.

Authors contributions

SLW: conception of the research, data collection, statistical analyses, writing and reviewing of manuscript; AMT: data collection and writing and reviewing of manuscript; MVIS: data collection and

manuscript collaboration; AEM: manuscript review; MASC: conception of the research and manuscript review.

Declaration of Conflicting Interests

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