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Factors associated with handgrip strenght loss in people living with hiv in use of antiretroviral therapy

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ABSTRACT

Background: To evaluate the frequency of reduction of handgrip strength (PGS) and its associated factors in people living with HIV using antiretroviral therapy.

Methods: A series of cases, carried out in a public hospital in Recife, PE, from March to July 2017, which evaluated patients ≥ 20 years, using a questionnaire that contained sociodemographic, anthropometric, clinical, biochemical and lifestyle variables. The handgrip strength test was performed using a dynamometer.

Results: A total of 109 patients were evaluated, of which 29.4% presented a reduction in the PGS. The female sex and schooling < 9 years were more likely to present a reduction in the PGS. Patients who had a CD4 cell count < 350 cells / mm³, and presented anorexia and fatigue presented a higher probability of reduction in PGS. There was no significant correlation between changes in anthropometric parameters and reduction in PGS. It is noteworthy to mention the observed frequency of underweight (10.2%) and overweight (49.1%) among subjects, as judged by their body mass index (BMI). In addition to the frequency of undernutrition by BMI, arm circumference, arm muscle circumference, triceps skinfold and percentage of weight loss were in the range of 30%.

Conclusion: Female gender, lower educational level, anorexia, fatigue and less number of TCD4 cells were associated with this reduction.

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KEY WORDS

Muscle Strength Dynamometer; Handgrip Strength; HIV; Antiretroviral Therapy; Nutritional Status.

INTRODUCTION

Acquired immunodeficiency syndrome (AIDS) is considered a public health problem. With various medical advancements in the treatment of this disease, including the emergence of antiretroviral therapy (ART), patients infected with the human immunodeficiency virus (HIV) have started to present greater suppression of viral replication, and consequently, greater survival rate. On the other hand, ART has potential side effects, which can contribute to a reduction in quality of life, including toxicity to treatment and changes in nutritional status[1].

Despite changes in the nutritional profile observed in recent years, studies show that a significant portion of people living with HIV (PLHIV) are still undernourished[2]. Therefore, both nutritional assessment and intervention in this population has become essential in order to improve the prognosis of these patients.

Nowadays, a simple and increasingly visible method is manual dynamometry or handgrip strength (PGS). Handgrip strength consists of the measurement of the maximum manual force with the aid of a dynamometer. This measurement evaluates the function of the skeletal muscle. It is a simple, non-invasive, low-cost method, and is described as one of the most sensitive functional tests that can indicate protein depletion[3].

Thus, the knowledge of the frequency of reduction in FPP and its associated factors in PLHIV using ART can help in the development of new strategies for the promotion, prevention and treatment of nutritional problems, aiming at improving the quality of life of these individuals.

OBJECTIVE

The aim of the present study was to analyze the handgrip strength and the factors associated with the reduction of handgrip strength in patients infected with the human immunodeficiency virus receiving antiretroviral therapy.

METHODS

Our team utilized an observational study of a series of cases conducted with PLHIV at the "Hospital das Clínicas" of the Federal University of Pernambuco (HC/UFPE). These PLHIV attended outpatient clinics during the period from March to June 2017. Male and female patients infected with HIV were receiving ART for at least 6 months in order to participate in this research. These subjects were at least 20 years of age and older. For the purpose of this study, we excluded pregnant women, patients who were unable to perform anthropometric measurements, patients who presented fluid retention (ascites and edema), as well as patients who had any cognitive deficit that would compromise their ability to participate in the current trial. However, among these patients who presented a cognitive deficit, there were participants that had reliable care givers. In these cases, the care givers responded to research questionnaires. Therefore those patients participated in the clinical trial.

The following data were also collected: socio-demographic data (sex, age, income, and education), clinical variables (time of diagnosis, time of ART, presence of fatigue and anorexia), biochemical variables (CD4 cell count and viral load), as well as nutritional variables. The nutritional variables that were evaluated consisted of: body mass index - BMI, percentage of weight loss -% PWL, PGS, arm circumference - AC, arm muscle circumference - AMC, waist circumference - WC, triceps skinfold - TSF). In addition, life style variables (smoking, alcoholism, physical activity) were also investigated.

Weight and height measurements were performed according to the original technique recommended by Lohman[4] Body mass index (BMI) was used to assess nutritional status according to the WHO classification[5]. The percent WL was calculated by the following formula: weight loss (%) = (usual weight - actual weight) x 100 ÷ usual weight, being classified according to Blackburn et al.[6]. Arm circumference (AC), AMC and TSF were measured according to Lohman[4], compared with the results of Frisancho[7] and classified according to Blackburn et al.[8].

The WC was obtained with an inelastic tape, with a precision of 0.1 cm. The tape was positioned directly on the skin at the midpoint between the last rib and the iliac crest[9]. In this study, WC was evaluated using WHO cutoff points as the standard reference[9].

The evaluation of the PGS was performed using a JAMAR® digital dynamometer. Participants received prior instructions regarding these procedures. In order to start the measurement, the patient was instructed to sit with hips and knees at 90° of flexion, shoulder at adduction, elbow flexed at 90°, with forearm and wrist in a neutral position. Three measurements were performed on the dominant hand, with duration period of 5 seconds for each attempt and an interval of 20 seconds between each attempt. These procedures were performed according to the recommendations of the American Society of Hand Therapists, in order to avoid muscular fatigue[10]. The results were recorded in kg/f and the largest measurement was used for classification. The classification was performed according to gender, and BMI as previously described by Evans et al.[11].

CD4 cell counts were categorized as >350 or ≤350 cells / mm³. These values were based on the classification of laboratory monitoring of PLHIV[12]. Viral load was classified as detectable (>40 copies) or undetectable viral load (≤40 copies).

Fatigue was assessed according to the Dutch Fatigue Scale (DUFS)[13]. This scale is composed of 8 items with likert responses of 5 points (1 to 5). Total DUFS scores can range from 8 to 40 and the presence of 'substantial fatigue' (or presence of fatigue) was defined when the total score was ≥ 14.5[14].

The evaluation of anorexia was performed using the Simplified Nutritional Appetite Questionnaire (SNAQ)[15].

To classify a patient's level of tobacco smoking, the following categories were considered: smoker (the individual who referred to currently smoking), non-smoker (the individual who never smoked), and former smoker (the individual who reported smoking at some point in their life, but did not smoke at the time of participation in the current research protocol).

In regard to alcohol consumption, the consumption of alcoholic beverages during the 30 days prior to the application of the questionnaire was evaluated. Dichotomous answers (yes or no) were considered.

The exercising levels were evaluated through the short version of the International Physical Activity Questionnaire (IPAQ). This questionnaire can classify the individual as sedentary, irregularly active, active and very active[16].

Statistical analysis was performed with version 13.0 of SPSS (Statistical Package for Social Sciences). In addition, version 7.0 of Stata software was used to evaluate the factors associated with the reduction of PGS. Furthermore, the Poisson regression model was used. Prevalence ratios were calculated using the robust method and the 95% confidence interval. The level of significance was 5%. All variables that presented $p<0.20$ in unadjusted bivariate analysis were selected for multivariate analysis using the *stepwise* method. Only the variables with a value of $p<0.05$ (significant) and between 0.05 and 0.10 (borderline) were left in the final model.

The protocol of this study was based on the ethical standards for research involving human beings, in accordance with the Resolution 466/12 of the National Health Council. This study design was approved (protocol CAAE: 62327716.0.0000.5208, opinion number: 1.929.918) by the Ethics and Research Committee on Human Beings of the Federal University of Pernambuco (UFPE). Individuals were previously informed of the research objectives, as well as of the adopted methods and signed the Free and Clarified Consent Term (FCCT).

RESULTS

The sample consisted of 109 individuals, with a mean age of 41.11 (± 11.46) years, of whom 67.0% were men, and 61.7% were in the age group between 20 and 44 years. Among the patients evaluated, 29.4% (n=32) presented reduced PGS (Table 1).

According to the bivariate analysis, it is observed that between the socio-demographic and lifestyle variables, the female sex and schooling £9 years were more likely to present

Table 1. Association of handgrip strength reduction with sociodemographic and lifestyle variables of people living with HIV using antiretroviral therapy. Recife, 2017.

Handgrip Strength Reduction									
Variables	Yes		No		Total		†PR	CI $_{95\%}$	P*
	N	%	N	%	N	%			
SEX									
Woman	15	41,7	21	58,3	36	33,0	1,79	1,01 - 3,16	0,048
Man	17	23,3	56	76,7	73	67,0	1,00	-	-
Total	32	29,4	77	70,6	109	100,0			
AGE (years)									
20 - 44	16	23,5	50	76,5	66	61,7	0,60	0,34 - 1,07	0,133
≥45	16	30,0	25	61,0	41	38,3	1,00	-	-
Total	32	29,9	75	70,1	107	100,0			
PER CAPITA INCOME (R$)									
≤1.000,00	17	31,5	37	68,5	54	50,9	1,26	0,68 - 2,33	0,599
>1.000,00	13	25,0	39	75	52	49,1	1,00	-	-
Total	30	28,3	76	71,7	106	100,0			
EDUCATION (years)									
≤ 9 years	21	43,8	27	56,3	48	46,2	3,06	1,49 - 6,27	0,002
>9 years	08	14,3	48	85,7	56	53,8	1,00	-	-
Total	29	27,9	75	72,1	104	100,0			
ALCOHOL CONSUMPTION									
Yes	11	21,6	40	78,4	51	47,2	0,61	0,33 - 1,16	0,180
No	20	35,1	37	64,9	57	52,8	1,00	-	-
Total	31	28,7	77	71,3	108	100,0			
TOBACCO SMOKING									
Smoker/Former smoker	12	28,6	30	71,4	42	38,5	0,96	0,52-1,75	0,941
Non-smoker	20	29,9	47	70,1	67	61,5	1,00	-	-
Total	32	29,4	77	70,6	109	100,0			
PHYSICAL ACTIVITY									
Sedentary/Irregularly active	03	20,0	12	80,0	15	13,8	0,65	0,23-1,86	0,545
Active/Very active	29	30,9	65	69,1	94	86,2	1,00	-	-
Total	32	29,4	77	70,6	109	100,0			

* Pearson's chi-square. †PR: Prevalence Ratio. CI $_{95\%}$: Confidence Interval of 95%.

a reduction in the PGS. The age and ethnicity variables were included in the regression model, as they presented p value <0.20 (Table 1).

Regarding clinical and biochemical variables, patients who had a CD4 cell count £ 350 cells / mm³, and presented anorexia and fatigue presented a higher probability of reduction in PGS (Table 2).

On the other hand, there was no significant correlation between changes in anthropometric parameters and reduction in PGS. Therefore, nutritional state of the patients had no statistical association with the reduction in PGS. Even though the statistical analysis did not find significant differences between the changes in nutritional state and reductions in PGS, it is noteworthy to mention the observed frequency of underweight (10.2%) and overweight (49.1%) among subjects, as judged by their BMI. In addition to the frequency of undernutrition, AC, AMC, TSF and % WL were in the range of 30% (Table 3).

In regard to the reduction of PGS, the results described by the Poisson regression as well as the adjusted effects of the

Table 2. Association of handgrip strength reduction and clinical and biochemical variables of people living with HIV using antiretroviral therapy. Recife, 2017.

	Palmar Grip Strength Reduction								
Variables	**Yes**		**No**		**Total**		**†PR**	**$CI_{95\%}$**	**P***
	N	**%**	**N**	**%**	**N**	**%**			
DIAGNOSTIC TIME (months)									
≤ 60	18	30,0	42	70,0	60	55,0	1,05	0,58 - 1.89	0,961
>60	14	28,6	35	71,4	49	45,0	1,00		
Total	32	29,4	77	70,6	109	100,0			
TIME OF USE OF ART (months)									
≤60	19	29,7	45	70,3	64	58,7	1,03	0,57 - 1,86	0,901
>60	13	28,9	32	71,1	45	41,3	1,00		
Total	32	29,4	77	70,6	109	100,0			
VIRAL CHARGE (copies)									
≤ 40	20	27,2	53	72,6	73	83,0	0,82	0,37 - 1,84	0,754
>40	05	33,3	10	66,7	15	17,0	1,00		
Total	25	28,4	63	71,6	88	100,0			
CD4 COUNT (cells / mm³)									
≤350	11	47,8	12	52,2	23	25,8	2,10	1,14 - 3,90	0,040
>350	15	22,7	51	77,3	66	74,2	1,00		
Total	26	29,2	63	70,8	89	100			
PRESENCE OF ANOREXIA									
Yes	11	47,8	12	52,2	23	21,1	1,96	1,11 - 3,45	0,053
No	21	24,4	65	75,6	86	78,9	1,00		
Total	32	29,4	77	70,6	109	100			
PRESENCE OF FATIGUE									
Yes	25	37,3	42	62,7	67	61,5	2,24	1,06 - 4,71	0,037
No	07	16,7	35	83,3	42	38,5	1,00		
Total	32	29,4	77	70,6	109	100			

* Pearson's chi-square. †PR: Prevalence Ratio. $CI_{95\%}$: Confidence Interval of 95%; ART: antiretroviral therapy.

Table 3. Association of the reduction of handgrip strength and anthropometric variables of people living with HIV using antiretroviral therapy. Recife, 2017.

Handgrip Strength Reduction									
Variables	**Yes**		**No**		**Total**		**†PR**	**CI $_{95\%}$**	**P***
	N	**%**	**N**	**%**	**N**	**%**			
BODY MASS INDEX									
Malnutrition	04	36,4	07	63,6	11	10,2	1,20	(0,50-2,91)	0,833
Eutrophy	12	27,3	32	72,7	44	40,7	0,90	(0,48-1,70)	
Excess	16	30,2	37	69,8	53	49,1	1,00		
Total	32	29,6	76	70,4	108	100			
WAIST CIRCUMFEREN									
Sem risco	18	24,3	56	75,7	74	74,0	0,63	(0,35 - 1,14)	0,211
Com risco	12	38,7	19	61,3	31	31,0	1,00		
Total	30	28,6	75	71,4	105	100,0			
ARM CIRCUMFERENCE									
Malnutrition	11	30,6	25	69,4	36	33,9	0,92	(0,38-2,19)	0,880
Eutrophy	15	27,3	40	72,7	55	51,9	0,82	(0,35-1,89)	
Excess	5	33,3	10	66,7	15	14,2	1,00		
Total	31	29,2	75	70,8	106	100			
ARM MUSCLE CIRCUMFERENCE									
Malnutrition	12	30,0	28	70,0	40	39,6	0,60	(0,28-1,31)	0,233
Eutrophy	12	23,5	39	76,5	51	50,5	0,47	(0,21-1,04)	
Excess	05	50,0	05	50,0	10	9,9	1,00		
Total	29	28,7	72	71,3	101	100			
TRICEPS SKINFOLD									
Malnutrition	11	28,2	28	71,8	39	36,8	1,08	(0,55-2,15)	0,486
Eutrophy	7	41,2	10	58,8	17	16,0	1,58	(0,76-3,31)	
Excess	13	26,0	37	74,0	50	47,2	1,00		
Total	31	29,2	75	70,8	106	100			
PERCENTAGE OF WEIGHT LOSS									
Yes	10	33,3	20	66,7	30	29,1	1,11	(0,60-2,05)	0,933
No	22	30,1	51	69,9	73	70,9	1,00		
Total	32	31,1	71	68,9	103	100			

* Pearson's chi-square. †PR: Prevalence Ratio. CI $_{95\%}$: Confidence Interval of 95%.

explanatory variables show an association between reduction of PGS and the following parameters: schooling £9 years (adjusted PR=2.49 p=0.000), CD4 count £350 (adjusted RP=1.67 p=0.020) and the presence of anorexia (adjusted PR=1.89 p=0.041). Two other variables presented borderline values after adjustment, such as: female gender (adjusted RP=1.38 p=0.067) and the presence of fatigue (adjusted RP=1.54 p=0.098) (Table 4).

DISCUSSION

The majority of the study population (67.0%) consisted of male participants, corroborating a study by Troche et al.[17], wherein authors observed a prevalence of 62% of male subjects among the studied population. In regard of age, the present studied population had an average of 41 years, similar to that found by Foresto et al.[18]. These authors determined that the average age was 45.5 years. Additionally, Silva et al.[19], described an average age of 41.1 years. These findings corroborate data available from the Ministry of Health[20] that shows a higher prevalence of HIV in men.

In our sample, we observed that females presented a higher probability of reduction in PGS, a variable that presented a borderline *p*-value after statistical adjustment. These findings corroborate other studies because these other studies show that men have higher PGS when compared to women[3]. According to these previously published studies, men usually have higher muscle mass due to their physiological characteristics. For instance, men present higher amounts of testosterone, growth hormone (GH) and insulin, which can contribute to the increase of both growth hormone 1 (IGF-1) and dehydropiandrosterone (DHEA). Their increased amounts of GH can enhance the turnover of muscle protein, and consequently, it can generate more muscle strength[3].

Study carried out with non-HIV-infected population described higher PGS among men (29.1) as compared to the women (19.8)[3]. Interestingly, Chilima & Ismail (2001)[24] observed an age-dependent decrease in these values in both sexes. On the other hand, we did not find an age-dependent reduction of PGS.

In relation to income levels, the majority of the studied population had a monthly income ≤ R$ 1,000.00 (51%). This population with a lower income was previously expected since the participants were attending a public hospital in Brazil. The PLHIV population who attend a public hospital in Brazil typically presents lower purchasing power, as also showed by Silva et al.[19]. Additionally, socioeconomic analysis demonstrated that 53.8% had more than 9 years of education. These results were different from the study of Schuelter-Trevisol et al.[21]. According to these authors, 80.1% of participants had less than 8 years of education in the PLHIV. Since the educational level is directly related to how PLHIV understand clinical procedures, the evaluation of the educational level is an important factor to be investigated among the PLHIV.

Regarding the studied factors that were potentially associated with the reduction of PGS, it was interesting to find that income level was not directly related to the reduction of PGS. However, patients who had an educational level £ 9 years did present a 2.49-fold higher probability of having a reduction of PGS. It is reasonable to suggest that this association found between educational level and the reduction of PGS could be explained by the fact that patient's lack of knowledge potentially associated with lower levels of education can directly interfere with the choice of treatment. The choice of ineffective treatment options can be also associated with more precarious living and health conditions[22]. More recently, a literature review presented an important take on how the non-HIV-infected pop-

Table 4. Ratio of gross and adjusted prevalence of factors associated with reduction in handgrip strength of people living with HIV using antiretroviral therapy. Recife, 2017.

Variables	Handgrip Strength Reduction					
	Gross PR †	$CI_{95\%}$	p	Adjusted PR †	$CI_{95\%}$	p
Women	1,79	1,01-3,16	0,048	1,38	0,97-2,11	0,067
Age 20 to 44 years	0,60	0,34-1,07	0,133	0,87	0,72-1,83	0,321
Education <9 years	3,06	1,49-6,27	0,002	2,49	1,74-3,65	0,000
Alcohol Consumption	0,61	0,33-1,16	0,180	0,48	0,93-2,35	0,142
CD4 count ≤350 cells/mm³	2,10	1,14-3,90	0,040	1,67	1,09-2,65	0,020
Presence of anorexia	1,96	1,11-3,45	0,053	1,89	1,10-2,42	0,041
Presence of fatigue	2,24	1,06-4,71	0,037	1,54	0,98-2,27	0,098

Poisson regression † PR: Prevalence Ratio. 95%CI: 95% Confidence Interval The variables with a value of p <0.05 (significant) and between 0.05 and 0.10 (borderline) were left in the final model.

ulation showed the lowest level of education and, this association was described as a risk factor for the reduction of PGS[23].

On the other hand, although previous findings studying a healthy population showed an association between PGS and level of physical activity[24], the current research protocol did not find a statistically significant association between these two factors. The underlying mechanism associated with the beneficial effect of physical activity on PGS could be due to the fact that physical activity stimuli are directly related to increased response of skeletal muscle. Therefore, this association would result in enhanced muscle mass and training resistance[24].

Furthermore, there was a greater proportion of CD4 cell counts (i.e. ≥ 350 cells / mm³), corroborating a study by Schuelter-Trevisol et al.[21], in which the authors found that 68.23% of PLHIV presented CD4 cell counts ≥ 350 cells / mm³. Additionally, studies performed in PLHIV show that there is an association between CD4 cell counts and nutritional state[24]. This association can be explained by the fact that the lower number of CD4 cell counts would characterize more advanced stages of infection, contributing to the appearance of opportunistic infections that can negatively influence nutritional state. This negative influence would be due to an increase in metabolism rate and a decrease in food intake[24]. The current study showed that individuals who presented lower CD4 cell counts would also have impaired performance in the PGS tests (adjusted PR=1.67 p=0.020).

An association between anorexia incidence and reduction of palmar grip strength were also observed after statistical adjustment. When anorexia is a consequence of a chronic disease, this eating disorder consists of a multifactorial problem and can be caused by inflammation of the hypothalamus. This inflammation seems to downregulates orexigenic hormones whilst upregulates anorexigenic. This pathological scenario can contribute to changes in nutritional state, which could cause the lower performance in the PGS test observed in the studied PLHIV[25,26].

Studies also suggest that fatigue is frequent in PLHIV. Fatigue has important clinical implications for the quality of life of these patients. The pathophysiology of fatigue has not yet been elucidated, and there are several theories for its origins. The most accepted theory is one that describes fatigue as a consequence of the deregulated levels of inflammatory cytokines[26]. In our research, the presence of fatigue was associated with reduced PGS (borderline). However, there are no studies in the literature that could corroborate this result. It is noteworthy to mention that the patients who presented fatigue most likely had lower physical performance, as well. Thus, it is reasonable to suggest that fatigue could have compromised nutritional state, and consequently caused the lower performance in the test with the dynamometer.

Surprisingly, anthropometric variables were not associated with PGS in the current studied population. These results cannot be corroborated with the literature, since several studies have shown that anthropometric variables are associated with PGS. A study conducted in Malawi with 94 adult and elderly non-HIV-infected individuals evaluated the relationship between nutritional state and PGS. This study showed a strong correlation between the increased PGS and increased muscle mass[21]. On the other hand, an inverse relationship between BMI was found by Hulens et al.[27]. In this case, lower peripheral muscle strength was observed in obese women when compared to eutrophic women. Therefore, these findings demonstrate a negative correlation between PGS and amount of body fat. A 2018 study also showed the relationship between PGS and nutritional status, but not as a measure to be performed in isolation[28]. Accordingly, one may consider that PGS can be positively associated with nutritional state[29].

Although our study failed to find an association between PGS and nutritional state, we observed a high frequency of both undernutrition and overnutrition, as judged by the BMI. Study participants did present a high prevalence of undernutrition as evidenced by AC, AMC, TSF and% WL, as well as a high percentage of reduced PGS when compared to the study published by Pinto et al.[30]. According to Pinto et al.[30], there is a prevalence of about 12.3% of PLHIV with reduced PGS. This shows that PLHIV using ART can present alterations in body composition due to both the HIV disease and associated treatment. These alterations in body composition include redistribution of body fat, decreased muscle mass and increased central adiposity. Additionally, lipodystrophy can also be commonly observed in these HIV-infected patients receiving ART. The presence of lipodystrophy may affect the measurements of TSF and AMC. Therefore, the prevalence of undernutrition and overnutrition should be cautiously interpreted in HIV-infected patients receiving ART. In addition, since PGS is a physiological measurement of nutritional state and it is unaffected by TARV[30], the analysis of PGS should be included in each clinical evaluation and follow-up of PLHIV.

Lastly, two limitations were identified in our study design. First, there is a lack of studies evaluating the causal relationship between PGS and all the variables studied in our PLHIV. Thus, we did not have specific cut-off points for this studied population. The second limitation was the restricted size of the sample. A restricted sample size can negatively influence the relationship between the studied variables and the PGS.

CONCLUSION

Although the majority of the population has adequate handgrip strength, it is possible to observe a growing percentage presenting handgrip strength reduction. Accordingly, it is important to perform handgrip strength testing during nutritional monitoring of people living with human immunodeficiency virus. Attention should be drawn to the people living with human immunodeficiency virus, as these individuals may present relevant body changes. Additionally, handgrip strength is one of the measurements used to evaluate both nutritional and overall health states, and also, handgrip strength is most likely not affected by the use of antiretroviral therapy. Lastly, in our study, females, lower levels of education, as well as patients presenting fatigue and anorexia exhibited reduced palmar grip strength.

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