Inflammatory markers as correlates of body composition and grip strength among adults with and without HIV: a cross-sectional study in Ethiopia

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Abbreviations

ART: antiretroviral therapy

BIA: bioelectrical impedance analysis

FFM: fat-free mass

FFMI: fat-free mass index

FM: fat mass

FMI: fat mass index

HIV: human immunodeficiency virus

s-AGP: serum alpha-1-acid glycoprotein

s-CRP: serum C-reactive protein

TBW: total body water

WHO: World Health Organisation

Abstract

Background: Changes in body composition and muscle strength are common among individuals with HIV. We investigated the associations of inflammation with body composition and grip strength in adults with and without HIV.

Methods: Cross-sectional study among Ethiopian treatment-naïve individuals with and without HIV. Fat mass and fat-free mass adjusted for height (kg/m^2) were used as indicators of body composition.

Results: 288/100 individuals with/without HIV were included between July 2010 and August 2012. Females with HIV had lower fat mass index **(**FMI) and fat-free mass index (FFMI) than females without HIV, whereas no difference was seen between males with and without HIV. Males and females with HIV had lower grip strength than their counterparts without HIV. Serum alpha-1-acid glycoprotein (s-AGP) was negatively correlated with FMI (-0.71 kg/m^2, 95% CI: -1.2; -0.3) among individuals with HIV, and those with HIV and serum C-reactive protein (s-CRP) ≥10 mg/l had 0.78 kg/m^2 (95% CI -1.4; -0.2) lower FMI than those with s-CRP <10 mg/l. In contrast, s-AGP was positively correlated with FMI (2.09 kg/m^2, 95% CI 0.6; 3.6) in individuals without HIV. S-CRP and AGP were negatively associated with grip strength in individuals with HIV, while no correlation was observed among those without HIV.

Conclusion: Inflammation was positively associated with FMI in individuals without HIV while it was negatively associated with FMI in those with HIV, indicating that inflammation may be one of the drivers of depleting energy reserves among treatment-naïve individuals with HIV. Inflammation was associated with decreased muscle quantity and functional capacity among individuals with HIV, but not in those without HIV.

Introduction

Among treatment-naïve individuals with HIV in sub-Saharan Africa, undernutrition is common and associated with systemic inflammation (1), a more rapid disease progression (2) and decreased survival (3, 4). Undernutrition and infections may lead to a vicious cycle, since undernourished individuals are more susceptible to HIV progression and opportunistic infections (2), while undernutrition among individuals with HIV may be exacerbated by decreased appetite or inadequate absorption of macronutrients (2, 5, 6). Substantial loss of fat-free mass in individuals with HIV may be driven by a cachectic process, while loss of fat mass (FM) may be a result of reduced energy intake and increased energy expenditure (7). Studies have indicated that the primary tissue lost may be explained by baseline fat content, as those with adequate fat stores lose predominantly FM, whereas those with low fat content tend to lose larger amounts of FFM (7-9). A study among undernourished (BMI <18.5 kg/m^2) individuals with HIV showed that systemic inflammation may play an important role in the regain of lost tissue after the initiation of antiretroviral therapy (ART), as reductions in C-reactive protein (CRP) in the early weeks of ART treatment were associated with higher gain of FFM (10). Systemic inflammation may also be associated with increased risk of functional decline, since both muscle mass (quantity) and muscle strength (functional capacity) may be decreased as a result of chronic systemic inflammation (11). The aim of this study was to investigate associations of inflammation with body composition and grip strength in ART-naïve individuals with HIV compared to individuals without HIV.

Methods

Study design, study population and setting

The study was a cross-sectional study using baseline data from the ARTfood study, which was a randomized controlled trial investigating the effects and feasibility of lipid-based nutrient supplementation in individuals with HIV at initiation of ART (12) (trial registration: ISRCTN32453477). In the present study, fat free mass index [FFMI; fat free mass (kg)/height (m^2)] and fat mass index [FMI; fat mass (kg)/height (m^2)] were used as height-adjusted indicators of body composition. Grip strength was an additional outcome variable as indicator of functional capacity (13, 14). Inflammation was assessed by CRP and alpha-1-acid glycoprotein (AGP).

Participants were recruited among individuals with HIV who were eligible for ART at Jimma University Specialised Hospital and the health centres in Jimma and Agaro, Oromia region, South-West Ethiopia. The inclusion criteria for the ARTfood study were age ≥18 years, ART-naïve, eligible for initiation of ART, and living within 50 km of the recruitment facility. Patients were excluded if they were pregnant, lactating, taking micronutrients or other nutrient supplementation. Eligibility of ART was based on the Ethiopian treatment guidelines from 2008: CD4 count ≤200 cells/µl irrespective of clinical symptoms, CD4 count ≤350 cells/µl if World Health Organisation (WHO) stage III, or WHO stage IV irrespective of CD4 count (15).

Additionally, an HIV negative reference group (n=100) was recruited from the voluntary testing and counselling service at Jimma University Specialised Hospital, and matched by age (±5 years) and sex with the last 100 recruited individuals with HIV.

Data collection

The study staff included nurses, laboratory technicians, and pharmacists, all receiving relevant training. Background data were collected by study nurses using structured questionnaires in the local languages Amharic or Afaan Oromo.

Anthropometry and body composition

For anthropometric measurements, participants were barefoot and wearing light clothes, and were asked to empty their pockets and remove any metal objects. A calibrated stadiometer (SECA 214 Stadiometer, Birmingham, UK) and scale (Tanita-BC 418 MA, Arlington Heights, USA) were used for height and weight, respectively. Weight was measured with 0.1 kg precision and height to the nearest millimetre. BMI was calculated as weight divided by height-squared (kg/m^2).

Body composition was measured using bioelectric impedance analysis. FM and FFM were directly derived from a single frequency 8-electrode body composition analyser using a constant frequency of 50 kHz (Tanita-BC 418 MA, Arlington Heights, USA) (16). We have previously published a validation of the manufacturers' equations against the deuterium dilution technique in this cohort (17). FM and FFM values were used to calculate FFMI and FMI (18). Bioelectrical impedance data were available for all participants recruited at Jimma University Specialised Hospital and the health centre in Jimma, but for logistic reasons data were not collected for all participants attending the health centre in Agaro.

Grip strength

Grip strength was measured using a digital grip dynamometer (Takei Scientific Instruments Co., Japan). The measurements were performed twice for the right and left hand carried out alternately and the highest of the two means was used for analyses.

Laboratory data

Haemoglobin was determined using an automated haematology analyser (Sysmex KX-21N, Kobe, Japan). Haemoglobin <7.75 mmol/l for women and <8.37 mmol/l for men defined anaemia, since standard cut-off values were adjusted +0.3 mmol/l accounting for the 1700 m altitude in the area (19).

CRP and AGP were measured in serum using an immunoturbidimetric assay (HORIBA ABX A11A01611) for Pentra 400 (HORIBA ABC, Montpellier, France). For s-CRP, the results are given in mg/l and the precision of the assay was 8.3 CV% based on repeated measurements of a normal serum in each run (mean ± SD: 0.71 ± 0.06 mg/l). For s-AGP, the results are given in g/l, and the precision of the assay was 3.4 CV% based on repeated measurements of a normal serum in each run (mean ± SD 0.69 ± 0.02 g/l). We defined elevated inflammation as s-CRP ≥10 mg/l or s-AGP ≥1.0 g/l.

Information regarding WHO clinical stage of HIV (20) was extracted from patient records and checked by a study clinician. CD4 cell count was determined in EDTA stabilised whole blood using flow cytometry (Facscount, Becton Dickinson, San José, USA). To determine viral load, plasma was kept at -80°C before quantification of HIV-1 viral load using a commercial Real Time PCR assay (RealTimeHIV-1, Abbott Laboratories, Illinois, USA) with automated extraction (M2000 Real Time System, Abbott Laboratories).

Data analysis

The collected data were double-entered and validated using Epidata (EpiData Association, Denmark). Data analyses were carried out using STATA/IC version 13.0 (StataCorp LP, USA). FFMI, FMI and grip strength were used as outcome variables. Multiple linear regression was used to assess associations between the inflammatory markers, AGP and CRP (as continuous and categorical variables), and body composition and grip strength, respectively. The distribution of all variables was tested, and skewed variables were reported as median with interquartile range (IQR), whereas normally distributed variables were reported as mean with standard deviation (SD). Models included adjustment for sex and age. In addition, tests of interaction between inflammation and HIV status were included in the models to assess whether the correlates of body composition and grip strength differed between individuals with and without HIV. Among individuals with HIV, test of interaction between inflammation and WHO stage (I, II, III and IV) was conducted to evaluate if the observed correlations differed between the different stages of disease severity. Results are presented as regression coefficients, β, with 95% confidence intervals. P-values <0.05 were considered significant.

Ethical statement

Written consent was obtained after the participants had received oral and written information about the purpose and methods of the study. The participants were informed that care and treatment were independent of study participation and that withdrawal from the study was allowed at any time. Study visits were coordinated with ART-related routine visits. In the case of additional visits, reimbursement was given to cover transportation costs. All data were handled anonymously and confidentially. Ethical approval was obtained from the Ethiopian National Health Research Ethical Review Committee and Jimma University Ethical Review Board. Trial authorisation was given by the Food, Medicine, and Health Care Administration and Control Authority of Ethiopia. A consultative approval was obtained from the Danish National Committee on Biomedical Research Ethics.

Results

Of 348 individuals with HIV enrolled in the ARTfood study between July 2010 and August 2012, bioelectrical impedance data were available for 288 (83%). These data were available for all the 100 participants without HIV. There was no difference in age, sex or BMI among individuals with HIV with and without bioelectrical impedance data (data not shown). Based on data obtained by the deuterium dilution technique, we found that there was no difference in FFM and FM among individuals with HIV with and without bioelectrical impedance data (data not shown).

Individuals with and without HIV had similar age, height, sex distribution and FFMI **(Table 1)**. Individuals with HIV had lower mean BMI compared to individuals without HIV (19.2 ± 2.6 vs. 21.4 ± 3.9, p<0.001). Haemoglobin levels were lower in individuals with HIV, and anaemia was observed in 46% of those with HIV, compared to 7% of those without HIV. Levels of inflammatory markers were higher in individuals with HIV compared to individuals without HIV. The median (IQR) s-CRP was 2.08 (0.5-7.1) mg/l and median (IQR) s-AGP was 0.95 (0.7-1.3) g/l among individuals with HIV, whereas median (IQR) CRP was 0.57 (0.2-2.5) mg/l and median (IQR) AGP was 0.63 (0.5-0.8) g/l among individuals without HIV (both p<0.001) (**Table 1**). Among individuals with HIV, CRP concentration increased slightly with disease progression. Those in WHO stage I and II had a median CRP of 1.2 mg/l, whereas CRP was 3.0 and 4.9 mg/l among those in WHO stage III and IV, respectively (p=0.04).

Considering body composition separately for men and women, women with HIV had lower mean (SD) FFMI (14.5 vs 15.3 kg/m^2, p=0.002) and mean (SD) FMI (4.2 ±2.0 vs 6.3 ±2.9 kg/m^2, p<0.001) compared to women without HIV, whereas men with and without HIV had similar BMI. Mean (SD) grip strength was 4.3 kg (20.5±4.0 vs 24.8±4.3 kg, p<0.001) lower among women with

HIV and 7.2 kg (28.7 ±6.5 vs 35.9 ±5.6, p<0.001) lower among men with HIV, compared to women and men without HIV, respectively (**Table 2**).

When assessing men and women combined, interactions were observed between HIV status and AGP (continuous variable) and between HIV status and CRP (categorical variable) for FMI. Higher AGP was associated with lower FMI among individuals with HIV and higher FMI among individuals without HIV (p for interaction <0.001) (**Table 3**). For each 1 g/l increase in s-AGP, FMI decreased by 0.7 kg/m^2 (95% CI -1.2; -0.3) in individuals with HIV, whereas FMI increased by 2.1 kg/m^2 (95% CI 0.6; 3.6) in individuals without HIV (**Table 3 and Figure 1**). Higher CRP was associated with lower FMI among individuals with HIV. For each mg/l increase in s-CRP, FMI decreased 0.01 kg/m^2 (95% CI -0.1 to -0.0). Among individuals with HIV, no interaction was observed between the WHO stages and the inflammatory markers. No associations between CRP and FMI were observed among individuals without HIV **(Table 3)**.

Individuals with HIV with CRP ≥10 mg/l had 0.8 kg/m^2 (95% CI -1.4 to -0.2) lower FMI compared to those with CRP <10 mg/l. No associations were seen between elevated CRP levels and body composition among individuals without HIV **(Table 3)**.

Among individuals with HIV, AGP ≥1.0 g/l were associated with -0.6 kg/m^2 (95% CI -1.1; -0.0) lower FFMI compared to individuals with HIV with AGP <1.0 g/l **(Table 3)**. In addition, inflammation was inversely associated with grip strength among individuals with HIV. A 1 g/l increase in s-AGP and 1 mg/l increase in s-CRP were associated with 2.7 kg (95% CI -3.5 to -1.3) and 0.03 kg (95% CI -0.5 to -0.0) lower grip strength, respectively. Those with HIV and AGP ≥ 1.0 g/l had 2.5 kg (95% CI -3.6; -1.3) lower grip strength compared to those with AGP <1.0 g/l. These associations were not seen in individuals without HIV. However, tests of interaction were insignificant indicating that HIV status did not modify the associations between inflammatory markers and grip strength **(Table 4)**.

Discussion

We observed interactions reflecting that the associations between markers of inflammation and body composition were different in those with and without HIV. Among individuals with HIV, inflammation was negatively associated with FMI and FFMI, whereas inflammation was positively associated with FMI in individuals without HIV. In addition, inflammation was negatively associated with grip strength in individuals with HIV, while no association was seen among those without HIV. Our findings highlight the role of systemic inflammation among ART-naïve HIV patients in relation to their body composition.

In the present study, the median CRP level was higher in individuals with HIV compared to individuals without HIV. Other studies have also reported higher CRP levels among individuals with HIV compared to individuals without HIV (21-23), but higher levels among individuals without HIV have also been observed (24). CRP levels observed in different studies varies remarkedly as it is affected by factors such as nutritional status, ART experience, and other chronic comorbidities or infections (10, 21, 23-25). In the present study the median s-CRP was 2.08 mg/l in individuals with HIV and the CRP concentration increased with disease progression. Despite a statistically significant difference in CRP across the WHO stages, we observed no clinically relevant difference in inflammatory markers (AGP and CRP) across the WHO stages. Several researchers have reported CRP levels (mean or median) below 5 mg/l (21, 24), whereas others have reported median CRP levels of 38.20 mg/l (10) and 61 mg/l (25) demonstrating the wide range of CRP levels observed among individuals with HIV.

Studies have shown that fat mass is positively associated with chronic inflammation in obese individuals (26-28). We found similar results in non-obese individuals without HIV, since increases in s-AGP were associated with higher FMI. In individuals with HIV, conversely, inflammation was negatively associated with FMI, with greater AGP negatively associated with FMI independent of disease severity. These results indicate that inflammation depletes energy reserves among individuals with HIV. Our findings are consistent with a study investigating the association of pathogen load with subcutaneous adipose tissue (central and peripheral), where pathogen load was estimated based on disability-adjusted life years due to infection (29). This study found that a higher pathogen load was associated with reduced central skinfolds, suggesting that stress of the immune system may affect central fat reserves more than peripheral adiposity.

Our findings also indicate that among individuals with HIV, inflammation may contribute to decreased muscle mass and/or muscle strength, since inflammation was negatively associated with FFMI and grip strength. These results are broadly consistent with a previous study assessing the effect of providing nutritional support to HIV-infected, ART-eligible adults in Tanzania and Zambia, where lower CRP levels shortly after ART initiation were associated with greater FFM gain (10).

It has been suggested that a functional measure of muscle strength is more important than the volume of FFM as a predictor of mortality (30). Results from our HIV cohort also suggests that strength is an important measure, particularly in men with HIV, who had 7 kg lower grip strength, but similar FFMI, compared to men without HIV. Among women with HIV, grip strength, FFMI and FMI were all lower compared to women without HIV.

The results demonstrate that muscle strength is decreased in both men and women with HIV, but to a larger extent in men. These sex differences may be explained by biological differences such as fat stores, physical strength and hormones. Men have a higher relative content of muscle, whereas women have a higher relative fat content (31). Additionally, there may be differences in the way men and women benefit from their body composition, when they are healthy or ill (32). These differences may be especially evident during the stress induced by infection. During illness, the body seems to sacrifice the tissue that in each sex is most important for reproduction, indicating a trade-off between survival and future reproduction (33), and this may account for the observed sex differences. It has been suggested that among individuals with HIV, women primarily lose FM (34) until the late stages of wasting when they also lose FFM (35), whereas men primarily lose FFM at all stages (34). Conversely, in a study of treatment for TB in Tanzania, adult males regained less fat and more FFM than females (32).

The strengths of the study include the HIV negative reference group that enabled comparison of individuals with and without HIV, and the validation of BIA against the deuterium dilution technique in the same HIV population (17). The cross-sectional study design is a limitation because a causal relationship between inflammation and body compositions as well as grip strength cannot be determined. Another limitation was the low level of inflammation among HIV negative individuals with inflammation, especially among men. There was also little variation in HIV severity in this population, because all participants were enrolled based on the ART eligibility criteria at the time of the study, which was prior to the adoption of WHO’s ‘test-and-treat’ recommendations (36). In Ethiopia, the 'test-and-treat strategy' was adopted in 2016. If these guidelines had been implemented at the time the study was conducted, the HIV cohort would probably have been more diverse, and individuals treated earlier might have had lower grade of inflammation and less depletion in fat mass, as well as muscle mass and functional capacity.

Conclusion

In this study we observed that the associations between inflammation and body composition was different in treatment-naïve individuals with HIV compared to a HIV negative reference group. Inflammation was positively associated with fat mass in individuals without HIV, as seen in obese individuals, whereas inflammation was negatively associated with fat mass in individuals with HIV. These results indicate that inflammation is one of the drivers of depleting energy reserves among treatment-naïve individuals with HIV. The results also indicate that functional capacity is an important outcome. The role of inflammation as a driver of energy depletion as well as loss of functional capacity should be investigated in future studies in order to qualify therapeutic recommendations.

Conflict of interest

Maria Hein Hegelund "no conflict of interest"

Jonathan Wells "no conflict of interest"

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Author Contribution Statement

MHH: performed statistical analyses and interpreted results, drafted and revised manuscript.

DFJ: Conceived the work, interpreted results, revised the manuscript and approved the final version.

AA: Acquired data, revised the manuscript and approved the final version.

DY: Acquired data, revised the manuscript and approved the final version

ÅBA: Designed the work, revised the manuscript and approved the final version.

DLC: Interpreted results, revised the manuscript, and approved the final version.

JWC: Interpreted results, revised the manuscript, and approved the final version.

TG: Designed the work, revised the manuscript and approved the final version.

HF: Designed and conceived the work, interpreted results, revised the manuscript, and approved the final version.

MFO: Designed and conceived the work, acquired data, interpreted results, revised the manuscript, and approved the final version.

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Figure legends

Figure 1: Association between alpha-1-acid-glycoprotein (AGP) and fat mass index between individuals with HIV (red line) and individuals without HIV (blue line).

Table 1. Characteristics of ART-naïve HIV positive and HIV negative Ethiopian adults.

	HIV positive (n=288)	HIV negative (n=100)	p-value
Socio-demographic characteristics			
Age, y	32.8 ± 8.9	30.9 ± 8.6	0.054
Women, n (%)	192 (66.7)	71 (71.0)	0.42
Education, n (%)			
No formal schooling	72 (25.0)	5 (5.0)	<0.001
Completed primary school	148 (51.4)	32 (32.0)	
Completed secondary school or higher	68 (23.6)	63 (63.0)	
Anthropometry			
Height, cm	160.3 ± 8.3	160.1 ± 8.0	0.86
Weight, kg	49.4 ± 7.8	54.7 ± 9.8	<0.001
BMI, kg/m^2	19.2 ± 2.6	21.4 ± 3.9	<0.001
<18.5	130 (45.2)	23 (23.0)	<0.001
18.5-24.9	136 (47.2)	58 (58.0)	
≥25	22 (7.6)	19 (19.0)	
Clinical characteristics			
Anaemia, n (%)	128 (46.0)	7 (7.1)	<0.001
C-reactive protein, median (IQR), mg/l	2.08 (0.5-7.1)	0.57 (0.2-2.5)	<0.001
<10 mg/l	230 (81.3)	91 (91.0)	0.02
≥10 mg/l	53 (18.7)	9 (9.0)	
Alpha-1-acid glycoprotein, median (IQR), g/l	0.95 (0.7-1.3)	0.63 (0.5-0.8)	<0.001
<1.0 g/l	161 (56.9)	91 (91.0)	<0.001
≥1.0 g/l	122 (43.1)	9 (9.0)	
HIV characteristics			
CD4 count, cells/µl			
< 50, n (%)	19 (6.8)		
50-100, n (%)	37 (13.2)		
>100-200, n (%)	104 (37.1)		
>200, n (%)	120 (42.9)		
Viral load, log(1+copies/mL)	4.8 ± 1.0		
WHO stage, n (%)			
Stage I	84 (29.7)		
Stage II	79 (27.9)		
Stage III	93 (32.9)		
Stage IV	27 (9.5)		

Values are means ± SD's, medians (IQR) and n (%).
Anemia was defined as hemoglobin (mmol/L) ≤7.75 (women) and ≤8.37 (men).

Table 2. Body composition and functional capacity of ART-naïve men and women with HIV and men and women without HIV from Ethiopia.

	Women (n=263)			Men (n=125)		
	HIV positive (n=192)	HIV negative (n=71)	p-value	HIV positive (N=96)	HIV negative (N=29)	p-value
Body composition						
Fat-free mass index (kg/m^2)	14.5 ± 1.8	15.3 ± 1.7	0.002	17.7 ± 3.0	17.3 ± 1.8	0.44
Fat mass index (kg/m^2)	4.2 ± 2.0	6.3 ± 2.9	<0.001	3.0 ± 1.7	3.6 ± 1.8	0.10
Functional capacity						
Grip strength, kg	20.5 ± 4.0	24.8 ± 4.3	<0.001	28.7 ± 6.5	35.9 ± 5.6	<0.001
Values are means ± SD. Body composition measured using bioelectrical impedance analysis.						

Table 3. Association between inflammation and body composition among 282 treatment-naïve HIV patients and 100 individuals without HIV.

	Fat-free mass index (kg/m^2)				Fat mass index (kg/m^2)			
	HIV positive	**HIV negative**	**Difference**	**P interaction**	**HIV positive**	**HIV negative**	**Difference**	**P interaction**
C-reactive protein, mg/l[a]	0.003 (-0.01; 0.1)	-0.004 (-0.01; 0.8)	-0.01 (-0.06; 0.03)	0.78	-0.01 (-0.02; -0.01)	0.01 (-0.03; 0.1)	0.03 (-0.02; 0.07)	0.28
< 10[b]	Ref.	Ref.			Ref.	Ref.		
≥10[b]	-0.41 (-0.2; 1.2)	0.76 (-0.7; 2.3)	0.35 (-1.29; 1.98)	0.68	-0.78 (-1.4; -0.2)	1.37 (-0.0; 2.8)	2.15 (0.61; 3.70)	0.01
Alpha-1-acid glycoprotein, g/l[a]	-0.31 (-0.79; 0.17)	1.09 (-0.5; 2.7)	1.40 (-0.23; 3.03)	0.09	-0.71 (-1.2; -0.3)	2.09 (0.6; 3.6)	2.81(1.28; 4.33)	<0.001
<1.0[b]	Ref.	Ref.			Ref.	Ref.		
≥ 1.0[b]	-0.56 (-1.1; -0.0)	0.37 (-1.1; 1.9)	0.93 (-0.65; 2.50)	0.25	-0.47 (-1.0; 0.02)	1.01 (-0.4; 2.4)	1.48 (-0.03: 2.98)	0.054

Correlates assessed using multiple linear regression adjusted for age and sex and with an interaction term between HIV status and inflammation. Analyses conducted for continuous and categorical variables of both inflammatory markers. All values presented as regression coefficients, β with 95% confidence intervals.

[a] Inflammation assessed as a continuous variable: β is the mean difference in FFMI or FMI for each one-unit increase in the inflammatory marker.

[b] Inflammation assessed as a categorical variable: β is the mean difference in FFMI or FMI compared to the reference group.

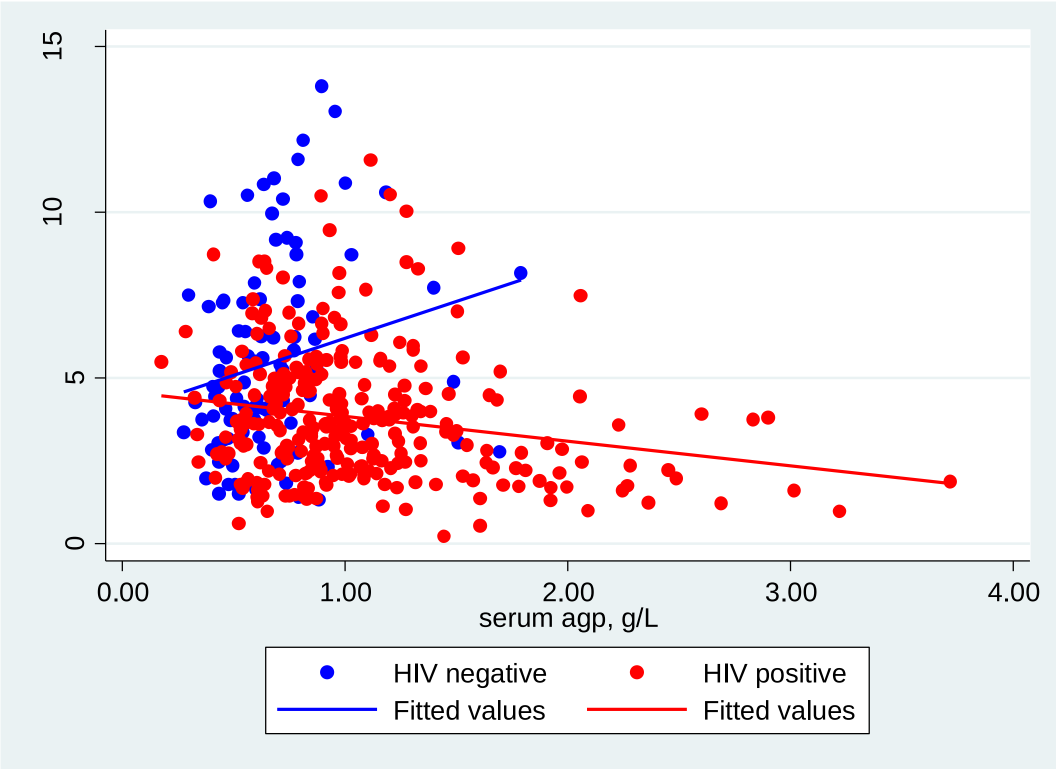
Table 4. Association between inflammation and grip strength among 282 treatment-naïve HIV patients and 100 individuals without HIV.

	Grip strength (kg)			
	HIV positive	**HIV negative**	**Difference**	**P interaction**
Inflammatory markers				
C-reactive protein, mg/l[a]	-0.03 (-0.5; -0.001)	0.03 (-0.07; 0.14)	0.06 (-0.05; 0.17)	0.29
< 10[b]	Ref.	Ref.		
≥10[b]	-1.00 (-2.24; 0.43)	-0.12 (-3.42; 3.18)	0.89 (-2.71; 4.48)	0.63
Alpha-1-acid glycoprotein, g/l[a]	-2.68 (-3.7; -1.7)	-0.45 (-3.5; 2.9)	2.23 (-1.25; 5.70)	0.21
<1.0[b]	Ref.	Ref.		
≥ 1.0[b]	-2.45 (-3.6; -1.3)	-1.23 (-4.5; 2.0)	1.22 (-2.19; 4.63)	0.48

Correlates assessed using multiple linear regression adjusted for age and sex and with an interaction term between HIV status and inflammation. Analyses conducted for continuous and categorical variables of both inflammatory markers. All values presented as regression coefficients, β with 95% confidence intervals.

[a] Inflammation assessed as a continuous variable: β is the mean difference in grip strength for each one-unit increase in the inflammatory marker.

[b] Inflammation assessed as a categorical variable: β is the mean difference in grip strength compared to the reference group.



15
10
5
0
0.00
1.00
2.00
3.00
4.00
serum agp, g/L
HIV negative
HIV positive
Fitted values
Fitted values