

## Original Research Article

# Study of factors affecting sarcopenia in PLHIV

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## ABSTRACT

**Background:** This study aims to determine the frequency of sarcopenia in PLHIV and determine the factors affecting sarcopenia in PLHIV.

**Methods:** The patients fulfilling the inclusion criteria were enrolled for the study after obtaining informed consent. Case record form was used to record relevant history. SARC-F (sluggishness, assistance in walking, rising from a chair, climbing stairs, falls) score is recorded by questionnaire. Hand grip strength and skeletal muscle mass index (SMI) were recorded. The correlation between grip strength and SMI with the duration of treatment in different regimens of HAART in PLHIV were studied. Possible factors affecting sarcopenia were determined based on history taken. All the parameters were compared between patients with and without sarcopenia. P value <0.05 was considered statistically significant. R version 4.1.2 statistical software was used for the statistical analysis.

**Results:** Sarcopenia was more commonly found in middle aged participants, who were less adherent to therapy, had a past history of tuberculosis, consumed alcohol, followed a vegetarian diet and did not exercise regularly.

**Conclusion:** Sarcopenia is more common in middle-aged individuals with long-term AIDS, especially those on prolonged ART. It's linked to non-adherence to ART, alcohol consumption, history of tuberculosis, and reduced physical activity. Strict adherence to ART, avoiding alcohol, increasing protein intake, and exercising regularly helps to combat this.

**Keywords:** Sarcopenia, PLHIV, Risk factors, HAART

## INTRODUCTION

Since the first recognition of HIV infection in 1981 in the US, the number of people living with HIV (PLHIV) has increased to 40.1 million adults worldwide as on July 2022, of which 21.4 lakh are Indians.<sup>1,2</sup> The total cases in India are 23.19 lakh in 2020. Overall, there was an estimate of 1,721 (1,361–2,210) PLHIV per million people in 2020 in India.<sup>3</sup> The infection has become four times more prevalent than it was in 1990. The life expectancy has more than doubled after the advent of Highly active antiretroviral therapy (HAART), making it a chronic disease rather than an acute infection.<sup>4</sup> The incidence of new cases has reduced by 40% between 2000 & 2016, attributed to preventive efforts and HAART. Sarcopenia is

defined as reduced skeletal muscle mass and either muscle strength or function.<sup>5</sup> Sarcopenia is suspected if the muscle strength is reduced and confirmed if skeletal muscle mass is reduced and considered severe if physical function is low.<sup>5</sup> Sarcopenia leads to poor physical function, quality of life, falls, fractures and dependency. The use of HAART has been associated with muscle mitochondrial damage and peripheral neuropathy.<sup>6</sup> However, the data on muscle mass and muscle strength in relation to HAART regimen and duration is inadequate. In this study, the frequency of sarcopenia in PLHIV, in the Indian population was determined. The factors causing sarcopenia like age, gender, ART drugs, adherence to treatment have been studied. Possible interventions to improve muscle strength and mass, could improve morbidity and mortality in PLHIV.

## METHODS

### *Study design*

Cross sectional study of 100 patients attending out-patient department as well as in-patients admitted to the Department of General Medicine of the hospitals attached to BMCRI.

### *Place of study*

Hospitals attached to Bangalore Medical College and Research Institute.

### *Study period*

Study duration was from February 2021 to august 2022.

### *Inclusion criteria*

Patients with age above 18 years who were diagnosed with HIV infection and willing to give informed consent were included in the study.

### *Exclusion criteria*

Patients with Age below 18 years and not willing to give informed consent were excluded from the study. Patients with clinical features of cerebrovascular, neurological or muscular diseases, known cases of diabetes mellitus, chronic liver disease, chronic kidney disease, hypothyroidism and hyperthyroidism and individuals taking anabolic drugs or supplements were excluded from the study.

### *Ethical approval*

After obtaining approval and clearance from the institutional ethics committee, the patients fulfilling the inclusion criteria were enrolled for the study after obtaining informed consent.

Case record form was used to record relevant history. SARC-F score is recorded by questionnaire. Hand grip strength and skeletal muscle mass index (SMI) were recorded. PLHIV, above 18 years of age, were screened for sarcopenia by SARC-F questionnaire and handgrip strength. Patients with a low SARC-F score (<4) or reduced handgrip strength are suspected to have sarcopenia. The diagnosis is confirmed by a reduced SMI. Hand grip strength was measured in kilograms (kg) by handgrip dynamometer.

Three measurements in each hand are taken and the maximum value was recorded. Skeletal muscle mass in kg by bioelectrical impedance analysis (BIA) machine was obtained. Height was measured in meters (m). Skeletal muscle mass index (SMI) in kg/m<sup>2</sup> is calculated by dividing skeletal muscle mass in kg by square of height (in m). Sarcopenia is diagnosed based on the guidelines of

European working group on sarcopenia in older people 2 (EWGSOP2), and from the reference values established from the study by Pal et al, in the Indian population. The correlation between grip strength and SMI with the duration of treatment in different regimens of HAART in PLHIV were studied. Possible factors affecting sarcopenia were determined based on history taken.

## RESULTS

A total of 100 participants were evaluated for sarcopenia and its associated factors. Among the participants 20% (n=20), were found to have sarcopenia. The baseline characteristics participants are as given below. Age distribution is as highlighted in Table 1. Majority of patients (n=12) with sarcopenia were between the age group 38 years to 57 years against those without sarcopenia (n=27), between 38 years to 47 years.

A total of 20 patients were found to have sarcopenia according to cut off value for SMI as per the study done by pal et al, in India. Maximum participants with sarcopenia were between the age 38 to 57 years. The mean age for the participant's having sarcopenia is 48 years, and for those without sarcopenia is 42 years, as given Table 2. The mean age was 41.7 years by a study done by Pinto et al.<sup>11</sup> The sex distribution is as shown in Table 3. Among the 100 participants studied 57% (n=57) were males and 43% (n=43) were females. Among males 21% (n=12) had sarcopenia, compared to 18.6% (n=12) among females.

The mean height and weight among participants with sarcopenia were 156 cm and 52 kg respectively, against a mean height of 160 cm and mean weight of 59.1 kg among those without sarcopenia. The mean height and weight are less among participants with sarcopenia as highlighted in Table 4. The distribution of the different drugs being taken is as given in Table 5.

Maximum participants were consuming ZLN (Zidovudine, Lamivudine, Nevirapine) (n=29) and ZLE (Zidovudine, Lamivudine, Efavirenz) (n=4) regimen of ART. Sarcopenia was more common among the group which was consuming ZLN regimen. The regimen was later changed to include TLD (Tenofovir, Lamivudine, Dolutegravir).

### *Factors affecting sarcopenia*

A total of 12% (n=12) of participants had tuberculosis. Tuberculosis was found to be present more commonly among participants with sarcopenia (30%, n=6), against 7.5% (n=6) than among those without sarcopenia as highlighted in Table 6. Total of 14% (n=14), were non adherent to ART. Among them 40% (n=8) were found to have sarcopenia compared to 7.5% (n=6) without sarcopenia, as shown in Table 7. Sarcopenia was found more commonly among participants who followed a mixed diet (60%, n=12) compared to those on vegetarian diet (40%, n=8), as shown in Table 8. More participants with sarcopenia consumed alcohol (25%, n=5), compared

to 17.5% (n=14) among those without sarcopenia. The result is statistically insignificant, as shown in Table 9. The participants with sarcopenia had HIV, and consumed ART

for a longer mean duration (7 years) compared to 5 years among those without sarcopenia, as shown in Table 10.

**Table 1: Age wise distribution of patients.**

	Sarcopenia						P value
	Absent		Present		Total		
Age (in years)	N	%	N	%	N	%	
18-27	10	12.50%		0.00%	10	10.00%	0.0985
28-37	18	22.50%	4	20.00%	22	22.00%	
38-47	27	33.75%	6	30.00%	33	33.00%	
48-57	17	21.25%	6	30.00%	23	23.00%	
58-67	8	10.00%	3	15.00%	11	11.00%	
68-77		0.00%	1	5.00%	1	1.00%	
Grand Total	80	100.00%	20	100.00%	100	100.00%	

**Table 2: Mean age distribution.**

	Sarcopenia						
	Absent		Present		Total		
	Mean	SD	Mean	SD	Mean	SD	P value
Age	42	12	48	12	43	12	0.035

**Table 3: Gender distribution.**

		Sarcopenia						
		Absent		Present		Total		
		Count	Column N %	Count	Column N %	Count	Column N %	
Sex	Female	35	43.80%	8	40.00%	43	43.00%	0.762
	Male	45	56.30%	12	60.00%	57	57.00%	

**Table 4: Distribution of height and weight.**

	Sarcopenia						
	Absent		Present		Total		
	Mean	SD	Mean	SD	Mean	SD	P value
Height (m)	1.6	0.1	1.56	0.08	1.59	0.1	0.087
Weight (kg)	59.1	11.2	52	8.2	57.7	11	0.009

**Table 5: frequency of sarcopenia based on drug regimen.**

		Sarcopenia						
		Absent		Present		Total		
		Count	Column N %	Count	Column N %	Count	Column N %	
ART	NAïVE	7	8.80%	4	20.00%	11	11.00%	0.008
	SLN/ZLN	0	0.00%	1	5.00%	1	1.00%	
	TLD	7	8.80%	0	0.00%	7	7.00%	
	TLE	3	3.80%	2	10.00%	5	5.00%	
	TLE/TLD	41	51.20%	3	15.00%	44	44.00%	
	ZLD	1	1.30%	0	0.00%	1	1.00%	
	ZLE/TLE/TLD	2	2.50%	0	0.00%	2	2.00%	
	ZLE/ZLN	1	1.30%	0	0.00%	1	1.00%	
	ZLE/ZLN/TLD	1	1.30%	0	0.00%	1	1.00%	
	ZLN	6	7.50%	0	0.00%	6	6.00%	
	ZLN/TLD	6	7.50%	7	35.00%	13	13.00%	
	ZLN/TLD/TLE	1	1.30%	1	5.00%	2	2.00%	
	ZLN/TLE/TLD	3	3.80%	2	10.00%	5	5.00%	
	ZLN/TZR	1	1.30%	0	0.00%	1	1.00%	

**Table 6: Frequency of sarcopenia in patients with tuberculosis history.**

		Sarcopenia						P value
		Absent		Present		Total		
		Count	Column N %	Count	Column N %	Count	Column N %	
TB	Absent	74	92.50%	14	70.00%	88	88.00%	0.006
	Present	6	7.50%	6	30.00%	12	12.00%	

**Table 7: Frequency of sarcopenia in ART adherent patients.**

		Sarcopenia						P value
		Absent		Present		Total		
		Count	Column N %	Count	Column N %	Count	Column N %	
Adherence	No	6	7.50%	8	40.00%	14	14.00%	0.0001
	Yes	74	92.50%	12	60.00%	86	86.00%	

**Table 8: Distribution of diet pattern.**

		Sarcopenia						P value
		Absent		Present		Total		
		Count	Column N %	Count	Column N %	Count	Column N %	
Diet	Mixed	68	85.00%	12	60.00%	80	80.00%	0.012
	Veg	12	15.00%	8	40.00%	20	20.00%	

**Table 9: Distribution in alcoholic and non-alcoholic patients.**

		Sarcopenia						P value
		Absent		Present		Total		
		Count	Column N %	Count	Column N %	Count	Column N %	
Alcohol	No	66	82.50%	15	75.00%	81	81.00%	0.444
	Yes	14	17.50%	5	25.00%	19	19.00%	

**Table 10: Distribution of disease duration for sarcopenia and non-sarcopenia patients.**

	Sarcopenia						
	Absent		Present		Total		P value
	Mean	SD	Mean	SD	Mean	SD	
Duration (in years)	5	4	7	4	6	4	0.092

## DISCUSSION

Human immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS) is currently considered a chronic disease due to the advances made in antiretroviral therapy (ART) in recent years.<sup>7</sup> As the prevalence of opportunistic infections decreased, there was an increase in the prevalence of chronic pathologies such as cardiovascular, liver, and kidney diseases, cognitive disorders, and osteoporosis.

This fact has generated speculations in relation to a probable “accelerated aging syndrome” in HIV-infected patients.<sup>8</sup> Several investigators have demonstrated bone mass loss and a greater fracture risk in HIV-infected patients. Whenever premature age-related comorbidities are detected in HIV-infected patients, it is crucial to evaluate the presence of sarcopenia, an important

condition responsible for an increased risk of falls and fractures that may ultimately lead to immobility and dependency. Indeed, sarcopenia may increase morbidity and mortality.<sup>9</sup> After the advent of cART, the lifespan of PLHIV has increased, thereby increasing the average age of PLHIV.<sup>10</sup> There are many postulations for sarcopenia occurring in HIV. One is the age factor due to increased longevity.

HIV causes muscle wasting due to myopathy or peripheral neuropathy, which may lead to AIDP, CIDP, mononeuritis multiplex and distal symmetrical polyneuropathy. The drugs in cART may have the side effects of peripheral neuropathy leading to wasting of muscles and sarcopenia. Drugs like stavudine and didanosine have been associated with peripheral neuropathy. Hence the drugs used for treating AIDS, can cause sarcopenia from mitochondrial injury.<sup>11</sup> Sarcopenia in HIV is also called the HIV wasting

syndrome which can either be due to the cytopathic effect of the virus itself or the drugs used to treat HIV. Hence, the advent of effective treatment against HIV has increased the prevalence of sarcopenia among PLHIV.<sup>12</sup>

Sarcopenia was found more commonly among participants of middle age between 38 years and 57 years, though this is statistically insignificant as the distribution of age is similar in participants without sarcopenia. However, sarcopenia was significantly associated with a higher mean age of 48 years.<sup>9</sup> More male participants were enrolled for the study, hence the association of sarcopenia with male sex is not statistically significant.

The participants with sarcopenia had a lower mean weight as expected due to wasting of skeletal muscle, along with a lower mean height. More participants with sarcopenia had consumed the ZLN (Zidovudine, Lamivudine, Nevirapine) regimen of ART, which was recently changed to TLD (Tenofovir, Lamivudine, Dolutegravir) regimen. Whereas, the participants without sarcopenia consumed the TLE (Tenofovir, lamivudine, Efavirenz) regimen which was changed to TLD, combination with Dolutegravir.

The duration of the disease and the duration of the ART was significantly associated with sarcopenia. The other factors that had a significant association with sarcopenia were past history of tuberculosis, vegetarian diet and not performing regular exercise or physical activity and also non-adherence to drug therapy. Hence, sarcopenia was more commonly found in middle aged participants, who were less adherent to therapy, had a past history of tuberculosis, consumed alcohol, followed a vegetarian diet and did not exercise regularly.

The term sarcopenia (sarx meaning flesh and penia poverty) was first proposed by Irwin Rosenberg in 1989 to describe the decline in muscle mass associated with age. Currently, the European Working Group on Sarcopenia in Older People (EWGSOP) has broadened this concept by including muscle strength and physical performance as additional diagnostic criteria, and proposing the stages presarcopenia, sarcopenia, and severe sarcopenia.

One of the primary limitations of this study is its cross-sectional design, which restricts the ability to establish causal relationships between the variables being examined. Additionally, the relatively small sample size may reduce the generalizability of the findings. With a larger and more diverse sample, it would be possible to obtain a more accurate representation of the broader population, increasing the robustness and external validity of the study.

## CONCLUSION

Sarcopenia has been found more commonly in middle aged participants who have the disease for a longer

duration and have consumed ART for a longer duration. This makes AIDS a chronic disease after the advent of ART, since the participants are aging with the disease. Therefore, they have been found to have sarcopenia. Since sarcopenia has been significantly associated with non-adherence to ART, consumption of alcohol and past history of tuberculosis, reduced physical activity the participants have been advised to be adherent to ART, restrain from consuming alcohol, have a diet richer in proteins, do regular exercise. Following the above advice helps reduce muscle wasting due to the disease and improve the patients skeletal muscle mass and strength, thereby reducing the presence of sarcopenia among PLHIV.

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*Ethical approval: The study was approved by the Institutional Ethics Committee*

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