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Evaluation of Osteosarcopenia and Biochemical Parameters in People Living with HIV

HIV ile Yaşayan Kişilerde Osteosarkopeni ve Biyokimyasal Parametrelerin Değerlendirilmesi

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ABSTRACT

Introduction: *In people living with HIV (PLWH), secondary issues may arise based on the disease itself or the treatments employed. Osteoporosis and sarcopenia are among these health issues, and in this study, our objective was to explore the occurrence of osteosarcopenia in PLWH. This is the first study to simultaneously investigate the co-occurrence of osteoporosis and sarcopenia in PLWH.*

Materials and Methods: *In our study, in which we examined the effect of HIV on osteoporosis and sarcopenia, volunteers between the ages of 18-65 who applied to the infectious diseases outpatient unit were included after obtaining approval from the ethics committee.*

Results: *Among the 50 patients, 44% did not have osteoporosis, while 50% had osteopenia, and 6% had osteoporosis. 10% of the patients had no sarcopenia, 34% had pre-sarcopenia, 40% had sarcopenia, and 16% had severe sarcopenia.*

Conclusion: *The detection of high levels of osteoporosis and sarcopenia in PLWH suggests that HIV disease or HIV-related risk factors have an impact on the musculoskeletal system. Although there was no significant relationship between osteoporosis and sarcopenia in our study, we found that patients with severe sarcopenia were more osteoporotic.*

Key Words: *HIV disease; Sarcopenia; Osteoporosis; Presarcopenia; Osteopenia*

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ÖZ

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Giriş: *HIV ile yaşayan bireylerde (HİYB) hastalığa veya kullanılan tedavilere bağlı olarak sekonder problemler ortaya çıkabilmektedir. Osteoporoz ve sarkopeni bu sağlık sorunlarından bazıları olup bu çalışmada HİYB'de osteosarkopeninin araştırılması amaçlanmıştır. Bu çalışma HİYB'de hem osteoporozu hem de sarkopeniyi birlikte inceleyen ilk çalışmadır.*

Materyal ve Metod: *HIV infeksiyonunun osteoporoz ve sarkopeni üzerine etkisini incelediğimiz çalışmamıza etik kurul onayı alındıktan sonra hastanemiz infeksiyon hastalıkları polikliniğine başvuran 18-65 yaş arası gönüllü HİYB'ler dahil edildi.*

Bulgular: *Çalışmaya dahil edilen 50 hastanın %44'ünde osteoporoz görülmezken, %50'sinde osteopeni ve %6'sında osteoporoz saptandı. Hastaların %10'unda sarkopeni yoktu, %34'ünde presarkopeni, %40'ında sarkopeni ve %16'sında şiddetli sarkopeni saptandı.*

Sonuç: *Çalışmamızda HİYB'de yüksek düzeyde osteoporoz ve sarkopeni saptanması, HIV hastalığı veya HIV ile ilişkili risk faktörlerinin kas-iskelet sistemini etkilediğini göstermektedir. Çalışmamızda osteoporoz ile sarkopeni arasında anlamlı bir ilişki bulunmamakla birlikte şiddetli sarkopenisi olan hastaların daha osteoporotik olduğu bulunmuştur.*

Anahtar Kelimeler: *HIV hastalığı; Sarkopeni; Osteoporoz; Presarkopeni; Osteopeni*

INTRODUCTION

With the introduction of highly active antiretroviral therapies (HAART), the life expectancy of people living with HIV (PLWH) has increased significantly. HIV has transformed from a fatal disease to a chronic disease[1-3]. Many health problems may occur in the chronic stage of HIV. Osteoporosis and sarcopenia are some of these health problems and may be associated with the disease itself or may occur due to medications used in treatment. Other risk factors of the host such as physical inactivity, low body mass index, malnutrition, lipoatrophy, insufficient calcium and vitamin D intake, smoking, alcohol, or opioid use, which are more common in PLWH, may increase the frequency of osteoporosis and sarcopenia[3,4].

Osteoporosis is a chronic disease of the skeletal system characterized by decreased bone mass and deterioration of its microstructure, resulting in increased bone fragility and fracture risk[5]. Similarly, sarcopenia is a progressive disease of the musculoskeletal system that can result in decreased muscle strength, muscle mass, physical performance, falls, fractures, and death[6]. Osteoporosis and sarcopenia may occur primarily due to aging, or secondary to causes such as endocrine, gastrointestinal, hematological, rheumatological, and genetic diseases, amyloidosis, sarcoidosis, heart failure, drugs, AIDS/HIV positivity, and weight loss[7]. Since muscle and bone cells originate from mesenchymal stem cells, a pathology that is a risk factor for osteoporosis may also be a risk factor for sarcopenia.

In PLWH, secondary problems may occur depending on the disease or the treatments used. Osteoporosis and sarcopenia are some of these health problems, and this is the first study that examines both osteoporosis and sarcopenia concomitantly in PLWH.

MATERIALS and METHODS

In our study, which examined the effect of HIV on osteoporosis and sarcopenia in PLWH, volunteers aged 18-65 years who applied to the infectious diseases outpatient unit after obtaining the approval of the ethics committee were included. The study was conducted in accordance with the Declaration of Helsinki, and written informed consent forms were obtained from all participants. Systemic and musculoskeletal physical examinations, routine blood tests, vitamin D, parathormone (PTH), serum electrolyte levels, anthropometric measurements, and DEXA tests of all participants were evaluated. Demographic data, body mass index, education level, marital

status, smoking and alcohol use, familial fracture history, previous fracture history, secondary systemic diseases, glucocorticoid use, 4-meter walk test, and chair stand up test values of the patients were recorded.

Diagnosis of Osteoporosis

The diagnosis of osteoporosis is made by measuring bone mineral density (BMD). According to the World Health Organization (WHO), osteoporosis is defined by a mean BMD measurement from the lumbar spine and hip with a T score equal to or less than -2.5 standard deviations in young adults, or when the Z score of individuals under 50 years old is equal to or lower than -2 standard deviations[8]. According to DEXA measurements of all individuals, those with a T score lower than -2.5 in the lumbar total (L1-L4) or any of the femoral neck regions are considered osteoporosis, those between -2.5 and -1 are considered osteopenia, and those above -1 are considered normal.

Diagnosis of Sarcopenia

According to the European Working Group on Sarcopenia in the Elderly (EWGSOP), muscle mass, muscle strength, and physical performance should be evaluated together for the diagnosis of sarcopenia. Muscle strength and physical performance are not affected, and a decrease in muscle mass is considered as "pre-sarcopenia", a decrease in muscle strength or physical performance with a decrease in muscle mass is considered as "sarcopenia", and a decrease in muscle mass, muscle strength, and overall physical performance is considered as "severe sarcopenia"[9].

For the evaluation of muscle strength, the hand grip strength of all individuals and the 5-repetition sit and stand test were evaluated. Physical performance was assessed with the 4-meter general walking speed test. In our study, muscle mass assessment was made with the DEXA measuring device, and the values of "Appendicular skeletal muscle mass, Appendicular skeletal muscle mass index" were recorded. In Table 1, reference cut-off values are given for the evaluation of muscle mass, muscle strength, and physical performance according to the EWGSOP-2 guidelines, and sarcopenia was evaluated based on these values in all participants[6].

Statistical Analysis

Analyses were evaluated using SPSS 22.0 software (Statistical Package for Social Sciences; SPSS Inc., Chicago, IL). In the study, descriptive data were presented as "n" and "%" values for categorical data and as "mean ± standard deviation (mean ± SD)" values for continuous data. Chi-square analysis (Pearson Chi-square) was used to compare categorical variables between groups. The normal distribution conformity of continuous variables was assessed using the Kolmogorov-Smirnov test. The Kruskal-Wallis test was used to compare more than two variables. The statistical significance level for the analyses was set at $p< 0.05$.

In the power analysis performed reference was made to the study by Pinto Neto et al. (human immunodeficiency virus infection and its association with sarcopenia) (presarcopenia was detected in 12.1% of HIV patients), using

Table 1. EWGSOP-2 sarcopenia reference values

Criterion	Measurement method	Reference value by gender
Muscle mass	Appendicular skeletal muscle mass Appendicular skeletal muscle mass index	Male: <20 kg 7 kg/m^2 Female: < 15kg 5.5 kg/m^2
Muscle strength	Hand grip strength Chair rising and sitting test	Male: <27 kg >15 seconds (5 times) Female: <16 kg >15 seconds (5 times)
Physical performance	4-meter walking speed	Male: ≤0.8 m/sn Female: ≤0.8 m/sn

the sample calculation with a certain universe (n= 140) n= [DEFF] *Np(1-p)]/[(d2/Z21-α/2*(N-1)+p*(1-p)]. It was determined that a minimum of 47 patients needed to be reached to achieve an 80% confidence interval, and this target was successfully reached.

RESULTS

A total of 50 patients, 44 (88%) male, and six (12%) female, were included in the study, with a mean age of 36.0 ± 10.9 (min= 18-max= 63) years. 62% of the patients were smokers. When the BMI (body mass index) categories of the patients were examined, 2% were underweight, 50% were of normal weight, 26% were overweight, 16% were obese, and 6% were morbidly obese. While 44% of patients did not have osteoporosis, 50% had osteopenia and 6% had osteoporosis. 10% of patients did not have sarcopenia, 34% had presarcopenia, 40% had sarcopenia, and 16% had severe sarcopenia. There was a moderate level of frailty in PLWH. The general characteristics, blood parameters and mean frailty levels of the patients are shown in Table 2.

Table 2. General characteristics of the patients

		Number	%
Age, mean ± SD		36.0 ± 10.9	
Gender	Male	44	88.0
	Female	6	12.0
Smoking	Yes	31	62.0
	No	19	38.0
BMI category	Underweight	1	2.0
	Normal	25	50.0
	Overweight	13	26.0
	Obese	8	16.0
	Morbid obese	3	6.0
BMI, mean ± SD		26.6 ± 6.3	
FMI, mean ± SD		8.9 ± 4.6	
Osteoporosis by DEXA T score	No osteoporosis	22	44.0
	Osteopenia	25	50.0
	Osteoporosis	3	6.0
Sarcopenia	No sarcopenia	5	10.0
	Presarcopenia	17	34.0
	Sarcopenia	20	40.0
	Severe sarcopenia	8	16.0
Vitamin D, mean ± SD		21.8 ± 8.2	
PTH, mean ± SD		45.5 ± 19.4	
Ca, mean ± SD		9.4 ± .4	
P, mean ± SD		3.4 ± .5	
Mg, mean ± SD		2.0 ± .1	
BMD, mean ± SD		.9 ± .1	
Frailty, mean ± SD		3.4 ± 2.3	
Treatment duration (months)		35.1 ± 31.5	

BMI: Body mass index, FMI: Fat mass index, PTH: Parathyroidhormone, BMD: Bone mineral density.

A significant negative difference was observed in terms of the presence of osteoporosis and BMI (p= 0.044). This difference resulted from the difference between the non-osteoporosis group and the osteoporotic group. The BMI values of patients with osteoporosis were found to be lower than those without osteoporosis. There was a significant difference between the presence of osteoporosis in terms of PTH (p= 0.005). This difference was due to the difference between the osteopenia and osteoporosis groups, and the PTH values of those with osteopenia were found to be higher than those with osteoporosis. There was a significant difference between the presence of osteoporosis in terms of BMD (p= 0.004). This difference was due to the difference between the non-osteoporosis group and the groups with osteopenia and osteoporosis. The BMD values of patients without osteoporosis were found to be higher than those with osteopenia and osteoporosis (Table 3).

The incidence of severe sarcopenia in smokers (19.4%) was significantly different from the rate of severe sarcopenia in non-smokers (10.5%) (p= 0.019) (Table 4).

While 4.5% of patients without osteoporosis had severe sarcopenia, 24% of those with osteopenia and 33.3% of those with osteoporosis had severe sarcopenia. There was no significant difference in the presence of osteoporosis concerning sarcopenia (p= 0.319) (Table 5).

DISCUSSION

It has become one of the important global health problems in the 21st century with the increasing number of patients and complications in PLWH. According to statistics made in 2021, 38 million people are living with HIV[10]. While the survival of PLWH was short before medical treatments were developed, life expectancy has increased significantly with the introduction of HAART[2], and HIV has been recognized as a chronic health problem by the World Health Organization.

Sarcopenia is characterized by a decline in muscle strength, muscle mass, or physical performance. Hormones that decrease with

Table 3. Comparison of all parameters according to the presence of osteoporosis

		No osteoporosis		Osteopenia		Osteoporosis		
		Mean ± SD		Mean ± SD		Mean ± SD		p*
Age		35.4 ± 10.7		35.7 ± 11.5		43.7 ± 6.8		0.348
Gender	Male	17	38.6	24	54.5	3	6.8	0.141**
	Female	5	83.3	1	16.7	0	.0	
Smoking	Yes	13	41.9	15	48.4	3	9.7	0.533**
	No	9	47.4	10	52.6	0	.0	
FMI		10.4 ± 6.1		8.1 ± 2.2		4.9 ± .7		0.077
BMI		28.6 ± 8.0[a]		25.6 ± 3.9[a.b]		20.4 ± .7[b]		0.044
Vitamin D		20.9 ± 9.1		21.6 ± 7.3		30.0 ± 4.5		0.193
PTH		38.5 ± 11.7[a.b]		54.3 ± 21.5[a]		24.4 ± 8.1[b]		0.005
Ca		9.4 ± .4		9.4 ± .4		9.2 ± .1		0.480
P		3.3 ± .5		3.5 ± .5		3.0 ± 1.1		0.269
Mg		2.0 ± .2		2.0 ± .1		2.0 ± .0		0.845
BMD		1.0 ± .1[a]		.9 ± .1[b]		.9 ± .1[a.b]		0.004
Frailty		3.6 ± 1.8		3.2 ± 2.8		3.0 ± 1.0		0.316
Treatment duration (months)		44.4 ± 37.7		28.8 ± 24.5		18.0 ± 12.0		0.315

a,b Group from which the difference originates.
*Kruskal Wallis analysis.
**Chi-square analysis was applied.
BMI: Body mass index, FMI: Fat mass index, PTH: Parathyroidhormone, BMD: Bone mineral density.

Table 4. Comparison of all parameters according to sacopenia class

		No sarcopenia		Presarcopenia		Sarcopenia		Severe sarcopenia		p*
		Num.	%	Num	%	Num	%	Num	%	
Age, mean ± SD		35.2 ± 10.3		33.4 ± 9.1		35.5 ± 11.3		43.6 ± 12.4		0.240
Smoking	Yes	2	6.5	9	29.0	14	45.2	6	19.4	0.019**
	No	3	15.8	8	42.1	6	31.6	2	10.5	
Gender	Male	2	4.5	16	36.4	18	40.9	8	18.2	0.471**
	Female	3	50.0	1	16.7	2	33.3	0	.0	
FMI, mean ± SD		11.9 ± 4.1		8.2 ± 3.5		9.1 ± 5.9		8.1 ± 2.5		0.127
BMI, mean ± SD		30.9 ± 5.2		25.7 ± 5.3		26.8 ± 7.8		25.8 ± 3.7		0.288
Vitamin D mean ± SD		18.4 ± 10.4		21.5 ± 7.4		21.2 ± 8.3		26.3 ± 7.9		0.359
PTH, mean ± SD		44.6 ± 16.6		42.5 ± 15.3		47.9 ± 23.0		46.7 ± 21.7		0.980
Ca, mean ± SD		9.5 ± .5		9.4 ± .5		9.4 ± .2		9.4 ± .6		0.872
P, mean ± SD		3.7 ± .6		3.3 ± .3		3.4 ± .6		3.3 ± .7		0.370
Mg, mean ± SD		2.0 ± .0		2.0 ± .2		2.0 ± .1		1.9 ± .1		0.682
BMD, mean ± SD		1.0 ± .1		.9 ± .1		.9 ± .1		.9 ± .1		0.153
Frailty, mean ± SD		3.0 ± 1.7		3.4 ± 3.0		3.8 ± 1.8		2.5 ± 1.9		0.210
Treatment duration (months)		44.2 ± 21.6		32.8 ± 34.0		40.3 ± 34.8		21.9 ± 20.9		0.364

*Kruskal Wallis analysis.
**Chi-square analysis was applied.
BMI: Body mass index, FMI: Fat mass index, PTH: Parathyroidhormone, BMD: Bone mineral density.

Table 5. Comparison of all parameters according to sacopenia class

	No sarcopenia		Presarcopenia		Sarcopenia		Severe sarcopenia		p*
	Number	%	Number	%	Number	%	Number	%	
No osteoporosis	3	13.6	8	36.4	10	45.5	1	4.5	0.319
Osteopenia	2	8.0	9	36.0	8	32.0	6	24.0	
Osteoporosis	0	.0	0	.0	2	66.7	1	33.3	

*Chi-square analysis was applied.

aging (growth hormone, insulin-like growth factor-1, corticosteroids, androgens, estrogens), proinflammatory cytokines that increase with chronic inflammation [Tumor necrosis factor-α (TNF-α), interleukin-1β (IL-1β), interleukin-6 (IL-6)] may cause the development of sarcopenia. In addition, it has been reported in many studies that muscle loss is observed as a result of malnutrition, immobility, trauma, exposure to reactive oxygen products, and increased oxidative stress[11,12]. There are many risk factors for the development of sarcopenia. HIV is one of these risk factors, and in our study, a certain level of sarcopenia was detected in 90% (34% of presarcopenia, 40% of sarcopenia, and 16% of severe sarcopenia) in PLWH. In the sarcopenia prevalence study conducted by Yazar et al. in Türkiye, the overall rate of sarcopenia was found to be 13.4%[13]. In a study conducted in Italy, the prevalence of sarcopenia was found to be 8.6%[14]. In our study, this rate was found to be 56%, and it is thought that the occurrence of sarcopenia at such a high level occurs due to the disease itself, drugs used, reactive oxygen products, malnutrition, chronic inflammatory process, or immobilization. In our study, when considering the factors influencing the development of sarcopenia, we observed that the incidence of severe sarcopenia was significantly higher among smokers compared to non-smokers. Our study is compatible with

the literature, and in a study conducted in Brazil, it was shown that smoking has an effect on the development of sarcopenia[15]. This significant difference may be due to the increase in exposure to reactive oxygen products and the catabolic effect of smoking. This shows that smoking is a risk factor for sarcopenia. Although male gender is seen as a risk factor in studies examining the relationship between sex and sarcopenia in the literature, we did not find a significant difference between men and women in our study. The inability to detect any differences in terms of gender may be attributed to the substantial number of male participants compared to the very limited number of female participants in our study.

With the increasing life expectancy among PLWH, there is a growing incidence of comorbidities, including osteoporosis and osteopenia. The treatment of these diseases is as important as the management of HIV. In addition to the known classical risk factors, HIV infection itself and the drugs used can also cause bone loss. In our study, while 44% of 50 naive PLWH did not have osteoporosis, 50% had osteopenia, and 6% had osteoporosis. In a meta-analysis by Brown et al., the decrease in bone mineral density was found to be between 12% and 62.5%, and in the same meta-analysis, osteopenia and osteoporosis rates were found to be 6.4 and 3.6 times higher than in the non-HIV-infected group[16]. Our study aligns with existing literature, and the mean occurrence of osteopenia and osteoporosis was determined to be 56%. Once again, in a study conducted on treatment-naive patients, Vlot et al. reported osteopenia in 44% of cases and osteoporosis in 11%, which is consistent with the findings in our study[17]. In our study, there was a significant difference between the presence of osteoporosis and BMD, and this difference was due to the difference between the groups without osteoporosis and those with osteopenia and osteoporosis. The BMD values of those without osteoporosis were found to be higher than those with osteopenia and osteoporosis. This was consistent with the literature, and we expected a decrease in BMD in patients with osteoporosis. Studies have found a negative correlation between obesity and osteoporosis[18]. Our study was consistent with the literature, and a negative significant difference was observed between osteoporosis and BMI (p= 0.044). The BMI values of those with osteoporosis were found to be significantly lower than those without osteoporosis. Although low vitamin D was found to be associated with osteoporosis and sarcopenia, we did not find any significant difference in our study. Again, we did not find a significant difference between other biochemical parameters and osteoporosis and sarcopenia.

In our study, the identification of elevated rates of osteoporosis and sarcopenia in PLWH suggests that HIV disease or HIV-related risk factors have an impact on the musculoskeletal system. While our study did not reveal a significant relationship between osteoporosis and sarcopenia, we did observe that patients with severe sarcopenia were more likely to have osteoporosis. This could be attributed to the fact that bone and muscle cells originate from the same origin.

CONCLUSION

In our study, we investigated the association between HIV and the presence of sarcopenia and osteoporosis. We examined the prevalence of sarcopenia and osteoporosis in PLWH as well as the contributing factors. Physical exercise and nutrition are significant factors in preventing potential musculoskeletal complications. Providing support and guidance throughout the treatment process can make a substantial difference. Therefore, it is essential for PLWH to receive education on adopting and sustaining healthy behaviors, including proper nutrition, hygiene, regular exercise, and adequate rest.

ETHICS COMMITTEE APPROVAL

This study was approved by the Harran University Clinical Research Ethics Committee (Decision no: HRÜ/22.23.35, Date: 28.11.2022).

CONFLICT of INTEREST

The authors have no conflicts of interest to declare that are relevant to the content of this article.

AUTHORSHIP CONTRIBUTIONS

Concept and Design: TM, ÇDT

Analysis/Interpretation: TM, ÇDT

Data Collection or Processing: TM, ÇDT

Writing: TM, ÇDT

Review and Correction: TM, ÇDT

Final Approval: TM

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