ASSOCIATION BETWEEN SERUM MYOSTATIN LEVELS AND SARCOPENIA IN MIDDLE-AGED ADULTS: A CROSS-SECTIONAL STUDY

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ABSTRACT

Introduction: Myostatin levels in individuals increase with age, resulting in reduced muscle mass and decreased strength, which contributes to the development of sarcopenia.

Objectives: To find and compare the levels of Myostatin in middle-aged Sarcopenic and non-Sarcopenic individuals.

Materials and Methods: Material and Methods: This cross-sectional study employed purposive sampling and was conducted in the Department of Physiology at Khyber Medical University from October 26, 2023, to March 19, 2024. The OpenEpi software was used to determine the sample size with 80% power and a 95% confidence level. Ninety-two volunteers (male=58, female=34) were included in the study, which used the SWAG-SARCO 2021. Myostatin levels were measured using an enzyme-linked immunosorbent assay. The exercise tests were performed in the skill labs at IBMS, KMU, and BKMC Mardan.

Results: A statistically significant difference ($p < 0.05$) was observed between the patients in the Sarcopenia group and those in the non-Sarcopenia group regarding MUAC, TSF, CC, height, weight, and BMI. In addition, a statistically significant difference ($p < 0.05$) was also found between the sarcopenia group and the non-sarcopenia group in terms of SPPB, Grip strength, IRM-Knee extension, weightlifting, Quad stretch, and TUG test. The mean myostatin levels between the sarcopenic and non-sarcopenic groups were also statistically significant ($p = 0.001$).

Conclusion: This study showed that even among middle-aged individuals, myostatin levels may increase, leading to an involuntary loss of skeletal muscle strength and mass known as sarcopenia.

Keywords: Myostatin, Sarcopenia, Muscle mass, Aging, Physical activity, Skeletal muscle mass.

INTRODUCTION

Sarcopenia is characterized by low muscle mass, which can significantly hinder the daily activities of those affected. The reported prevalence of sarcopenia in the elderly population is approximately 10-16% worldwide [1], and quite a high prevalence of more than 40% in Pakistan in older adults highlights the significance of early screening [2]. Effective management and ongoing follow-up are crucial for improving the quality of life for individuals experiencing sarcopenia.

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The management of sarcopenia depends on age and disease stage. Both non-pharmacological and pharmacological approaches exist to address it. Non-pharmacological approaches include dietary management and resistance exercises [3]. These resistance exercises are recommended as the first-line treatment for managing sarcopenia. Reduced physical mobility can lead to increased fat storage in muscles, thereby worsening the signs and symptoms of sarcopenia [4].

Sarcopenia means a reduction in skeletal muscle mass and strength [5]. Myostatin is a protein found in muscles and encoded by the MSTN gene [6]. As individuals age, their levels may increase, which can lead to reduced muscle mass and strength while contributing to the development of sarcopenia. As the symptoms of sarcopenia become more pronounced, myostatin levels rise concurrently. Numerous factors regulate myostatin levels in the body, including age, mutations, hormonal regulation, inflammatory conditions, sleep, stress, and diet [6,7]. This phenomenon commonly manifests with age, yet recent

research indicates it can occur in younger age individuals [8].

Characterized by slow and gradual progression, Sarcopenia necessitates early intervention to mitigate its effects before widespread manifestation within the body [9]. Diagnosis of Sarcopenia typically relies on the observation of three primary traits: skeletal muscle strength, quality, and quantity, along with physical performance [9,10]. Such degenerative conditions not only disrupt daily activities but also significantly influence postoperative outcomes, leading to heightened complication rates and increased morbidity and mortality, particularly in major surgical procedures involving skeletal muscles. Numerous factors regulate myostatin levels in the body, including age, mutations, hormonal regulation, inflammatory conditions, sleep, stress, and diet [7]. Skeletal muscle loss begins at 35 years of age, occurring at 1–2% every year. Muscle loss increases to 3% per year after 65 years [11].

As so far not much work has been done to investigate the condition in the younger age group, this study investigates whether myostatin plays a role in causing sarcopenia in adults aged 35 to 50 in Pakistan.

MATERIAL AND METHODS

This cross-sectional study employed a purposive sampling method from October 26, 2023, to March 19, 2024. After review and approval by the Graduate Study Committee, the Advanced Study and Research Board approved the proposal under letter No. DIR/KMU-AS&RB/AB/002274, dated July 23, 2024, as well as the Ethical Board No. 9297/PGMED/KGMC. The study and all experimental work were conducted in the Department of Physiology at the Institute of Basic Medical Sciences (IBMS) of Khyber Medical University (KMU), Peshawar, Pakistan. The OpenEpi software was employed to determine the sample size with 80% power and a 95% confidence interval. The mean and SD of Myostatin levels in individuals with sarcopenia compared to those without sarcopenia. Myostatin levels were measured using an enzyme-linked immunosorbent assay. The sample size was calculated from Alice *et al.,* 2021 [12]. We kept the power 80% and 95% confidence intervals and used the Mean and SD of Myostatin in Sarcopenia (120.6 ± 13.7) versus non-sarcopenia individuals (48.8 ± 11.6). The sample was calculated to be 89, but we enrolled 92 volunteer participants.

Following informed consent, ninety-two volunteers (58 males and 34 females) were screened for sarcopenia using the SWAG-SARCO 2021. Blood samples were taken, and history, anthropometric measurements, and exercise tests were performed in the skill labs of IBMS, KMU, and Bacha Khan Medical College in Mardan, using digital scales, measuring tapes, and skinfold callipers. The International Physical Activity Questionnaire (IPAQ) was used to assess participants' baseline levels of physical activity [13]. Myostatin levels were measured using an enzyme-linked immunosorbent assay [14]. The mean and SD of Myostatin levels in individuals with sarcopenia compared to those without sarcopenia.

Adults aged 35 to 50 with a sedentary lifestyle participated in the study. Excluded were those with diabetes, hypertension, hypothyroidism, Parkinson's disease, stroke, severe arthritis, recent surgery, pregnancy or lactation, or those taking medications such as steroids.

The statistical analysis was conducted using SPSS version 24. Descriptive statistics were calculated to summarize the data, including the means and standard deviations of the continuous variables. To compare the groups, an independent-sample t-test was applied.

RESULTS

The normality of the data, as determined by the Shapiro-Wilk test, indicated a normal distribution. Of the 92 volunteers screened and recruited via purposive sampling, 63 were Sarcopenic, and 29 were non-Sarcopenic (male =58, female = 34). The mean age of the participants was 41.90 ± 4.584 years.

A statistically significant difference ($p < 0.05$) was observed between the patients in the Sarcopenia group and those in the non-Sarcopenia group regarding MUAC, TSF, CC, height, weight, and BMI, as shown in Table 1.

Table 1: Comparison of Anthropometrics between Sarcopenic and Non-Sarcopenic Groups

Parameters	Sarcopenic Mean±SD (95%CI)	Non-Sarcopenic Mean±SD (95%CI)	p-value
MUAC (cm)	18.96±2.011 (16.9, 20.9)	29.09±3.231 (25.8, 32.3)	**0.001**
TSF (mm)	9.80±1.628 (8.2, 11.4)	17.91±2.755 (15.2, 20.6)	**0.003**
WC (inches)	27.23±4.011 (23, 31)	39.21±3.927 (35, 43)	0.347
Height (cm)	159.63 ± 12.661 (147, 172)	141.63±5.341 (136.3, 147)	0.702
CC (inches)	28.80 ±2.372 (26.4, 31.2)	35.74 ± 2.092 (33.7, 37.8)	**0.001**
Body Mass Index (BMI)	24.5 ± 4.22 (20.3, 28.7)	33.29 ± 5.748 (27.5, 39)	**0.002**
Weight (kg)	68.8 ± 8.15 (60.7, 77)	83.38 ± 5.26 (78, 89)	**0.001**

Mid Upper Arm Circumference = MUAC, Triceps Skinfold Thickness = TSF, Waist Circumference = WC, Hip Circumference = HC, and Calf Circumference = CC

A statistically significant difference ($p < 0.05$) was found between the sarcopenia group and the non-sarcopenia group in terms of SPPB, Grip strength, IRM-Knee extension, weightlifting, Quad stretch, and TUG test.

Table 2: Comparison of physical performance parameters between Sarcopenic and Non-Sarcopenic Groups.

	Sarcopenic Mean± SD (95%CI)	Non Sarcopenic Mean± SD (95%CI)	p-value
SPPB	5.67±1.3 (4.37, 6.97)	11.74±1.7 (10, 13.4)	**0.001**
SARC-F Score (n)	4.30±2 (2.30, 6.3)	3.98±2.2 (1.78, 6.18)	0.456
Grip Strength (kg)	22± 3.4 (18.6, 25.4)	40.72± 4.7 (36, 45.4)	**0.003**
IRM- Knee Extension	2.61±1.2 (1.4, 3.8)	7.87±1.2 (6.7, 9.07)	**0.004**
Weightlifting (sec)	16.7± 2.5 (14.2, 19.2)	26.8±2.4 (24.4, 29.2)	**0.004**
Dead Hang (sec)	1.46±0.5 (0.96, 1.96)	1.39±0.5 (0.89, 1.89)	0.532
Air Squats (sec)	62.39±13.63 (48.76, 76.02)	29.61±6.832 (22.78, 36.44)	0.668
Quad Stretch (sec)	6.4 ±2.021 (4.38, 8.42)	33.15±4.85 (28.3, 38)	**0.004**
Gait Speed(m/s)	1.42±0.361 (1.06, 1.78)	2.45 ±0.611 (1.84, 3.06)	0.215
TUG test (sec)	11.70 ±1.641 (10.06, 13.34)	7.22 ±2.742 (4.48, 9.96)	**0.004**
5 times Sit to Stand Test(sec)	13.70 ±2.481 (11.22, 16.18)	9.22 ±4.746 (4.47, 13.97)	0.552

30-second Chair stand test (rep)	12.82 ±2.06 (10.76, 14.88)	33.62 ±2.743 (30.88, 36.36)	0.163

SPPB = Short Physical Performance Battery
SARC-F = strength, assistance in walking, rising from the chair, climbing stairs, and falls
IRM knee extension = One Repetition Maximum Knee Extension
Quad stretch = Quadriceps muscle stretch
TUG test = time up and go test

The bar graph compares mean myostatin levels between sarcopenic and non-sarcopenic groups. The p-value for the difference between the two groups is 0.001, indicating a statistically significant difference (Figure 1).

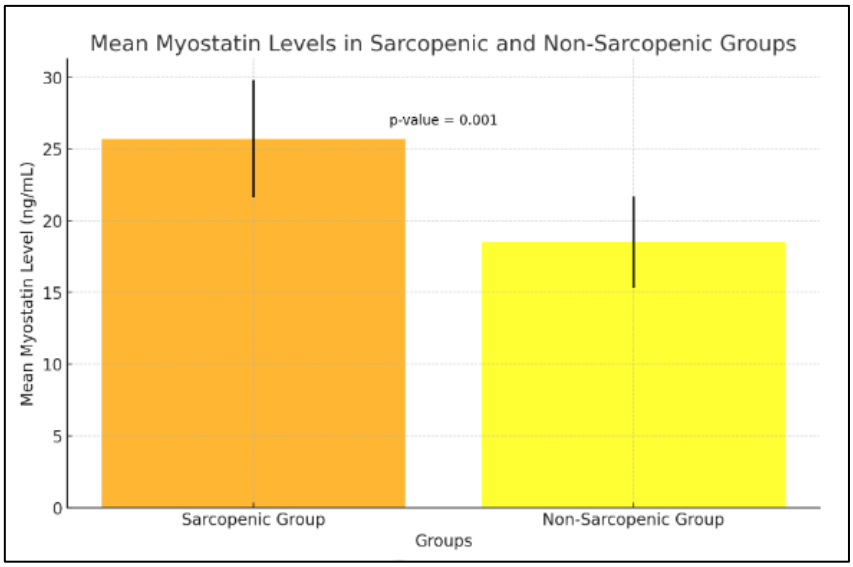

Figure 1: Comparison of Mean Myostatin Levels between Sarcopenic and Non-Sarcopenic Groups

DISCUSSION

Overall, our findings showed statistically significant differences in anthropometric measurements, physical performance parameters, and Myostatin levels between the Sarcopenia and the non-Sarcopenia group. The study demonstrated a statistically significant difference in MUAC, TSF, and CC between Sarcopenic and Non-Sarcopenic individuals ($p < 0.05$). These anthropometric markers are crucial indicators of muscle mass and nutritional status, with lower values in Sarcopenic patients indicating diminished muscle reserves and potential malnutrition. This is consistent with Ren *et al.,* 2022, who reported similar associations between reduced MUAC and increased prevalence of Sarcopenia in older adults in Europe [15]. Additionally, a study by Landi *et al.,* 2022 found that lower calf circumference strongly correlates with decreased muscle strength and function, further supporting the current findings [16].

However, no significant differences were observed in waist and hip circumference between the groups ($p > 0.05$). This suggests that central adiposity between Sarcopenic and non-sarcopenic individuals may not differ markedly, while peripheral muscle wasting is more pronounced, as supported by Park *et al.,* 2023 [17]. Lower muscle mass in Sarcopenic individuals is a hallmark of the condition [18,19].

The SPPB, which evaluates lower-extremity function, showed significantly poorer scores in the Sarcopenic group. This is consistent with research by González *et al.,* 2024 who showed SPPB as a reliable predictor of disability and mobility issues in older adults [20]. The IPAQ results indicated lower physical activity levels in Sarcopenic individuals, which is corroborated by studies by Bilski *et al.,*2022, and Araújo *et al.,*2025, highlighting the role of reduced physical activity in the progression of Sarcopenia [4,21]. The SARC-F score, while helpful for screening, may lack sensitivity in differentiating between varying severities of Sarcopenia.

The study also highlighted significant differences in Grip Strength, One-Repetition Maximum Knee Extension, and Weightlifting between the groups, with Sarcopenic individuals showing markedly reduced performance ($p < 0.05$). Grip strength, a proxy for overall muscle strength, was notably lower in the Sarcopenic group, consistent with findings by Cawthon *et al*., 2020, who identified grip strength as a critical marker of Sarcopenia and a predictor of adverse outcomes such as disability and mortality [22]. The lower performance in weightlifting and knee extension exercises further underscores the diminished muscle power in Sarcopenic individuals. These findings are supported by research from Zhang *et al.,* 2020, which demonstrated similar declines in muscle strength and function with aging and Sarcopenia [23].

Myostatin levels were higher in Sarcopenic individuals and have been associated with muscle wasting and Sarcopenia [6,7]. These findings are consistent with earlier reports and suggest that targeting Myostatin could be a potential therapeutic approach to mitigating Sarcopenia

The TUG test is widely used to assess mobility, balance, walking ability, and fall risk, with slower times indicating more significant impairment. Similar results were reported by Sakthivadivel *et al.,* 2022 and McLay *et al.,* 2020 [24,25].

The study also found statistically significant differences in body composition and muscle mass between Sarcopenic and Non-Sarcopenic individuals. These findings align with research by Li CW *et al*., 2022 [26]. The reduced muscle mass in Sarcopenic individuals also align with findings from Nishikawa *et al*., 2021, who reported that Sarcopenic patients have significantly decreased muscle mass [27].

Our study found that sarcopenic patients had significantly higher levels of myostatin than their non-sarcopenic counterparts. Our results align with Seo *et al.,* 2020 [28]. Myostatin, a negative regulator of muscle growth, plays a crucial role in the pathophysiology of sarcopenia. This finding supports the well-established role of myostatin in muscle wasting and deterioration associated with sarcopenia. Sarcopenic patients with elevated myostatin levels demonstrated lower MUAC, TSF, and CC measurements [29.]

Sarcopenic patients with elevated myostatin levels exhibited lower values for bone mass, hydration status, protein percentage, basal metabolic rate (BMR), and muscle mass [30]. These results highlight the broad impact of myostatin on body composition and metabolism, aligning with findings from studies reporting myostatin's role in muscle and bone degradation [31]. The significant differences in these parameters reinforce the relationship between high myostatin levels and adverse changes in body composition, often seen in sarcopenic patients.

CONCLUSIONS

The observed differences in muscle strength, functional mobility, and biochemical markers between Sarcopenic and Non-Sarcopenic individuals highlight the importance of early detection and management of Sarcopenia. Interventions such as resistance training, optimized nutrition, and novel pharmacological strategies targeting Myostatin may offer promising options for slowing disease progression. Longitudinal studies may help better understand the natural course of Sarcopenia and assess the safety and effectiveness of targeted therapies, including Myostatin inhibition.

Limitations

1) The sample size was small due to financial limitations.

2) Although myostatin alone has been discussed in relation to sarcopenia, further studies involving two or more factors can provide a broader overview.

3) The study enrolled only middle-aged individuals.

Authors' Contributions

Author Name	Contribution
Dr. Mahwish Israr	Conception and design of the study, critical appraisal of the Manuscript and data analysis
Dr. Zubia Shah	Conception and design of the study, data collection, critical appraisal, and preparation of the manuscript
Dr. Muhammad Omar Malik	Conception and design of the study, and data analysis
Dr. Farida Ahmad	Data collection, critical appraisal of the manuscript

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