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The Association between Serum Uric Acid Levels and Muscle Strength in the Elderly Population of Amirkola

S. R. Hosseini (MD, MPH)[*1], A. Bahrami (MD)[2], F. Pourabdolhossein (PhD)[3], R. Jokar (MD)[4], R. Ghadimi (MD, PhD)[1], A. Bijani (MD, PhD)[1]

1.Social Determinants of Health Research Center, Health Research Institute, Babol University of Medical Sciences, Babol, I.R.Iran.
2.Student Research Committee, Babol University of Medical Sciences, Babol, I.R.Iran.
3.Cellular and Molecular Biology Research Center, Health Research Institute, Babol University of Medical Sciences, Babol, I.R.Iran.
4.Clinical Research Development Unite of Rouhani Hospital, Babol University of Medical Sciences, Babol, I.R.Iran.

•**Corresponding Author: S. R. Hosseini (MD, MPH)**
Address: Social Determinants of Health Research Center, Health Research Institute, Babol University of Medical Sciences, Babol, I.R.Iran.
Tel: +98 (11) 32199936. **E-mail:** hosseinirezaseyed@gmail.com

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ABSTRACT

Background and Objective: As an antioxidant, uric acid may play an important role in preventing the decline of muscle strength and mass in the elderly. The results of studies conducted to date have not been conclusive and have mostly focused on the relationship between handgrip strength and serum uric acid levels. The aim of this study is to determine the association between serum uric acid levels and hand and quadriceps muscle strength in the elderly.

Methods: This cross-sectional study was part of the second phase of the Amirkola Health and Aging Project (AHAP) cohort study, which was conducted randomly on 800 elderly individuals. Hand muscle strength was measured using a digital hand dynamometer, and quadriceps muscle strength was measured using a handheld dynamometer, which was secured on one side by a band above the ankle and on the other side by a spring scale attached beneath the chair, in kilograms. Serum uric acid levels were measured using an autoanalyzer in milligrams per deciliter.

Findings: The mean age of the study participants was 69.74±7.14 years; 448 (56%) of the elderly were male and 352 (44%) were female. In this study, with increasing serum uric acid levels, the mean hand and quadriceps muscle strength increased significantly ($p<0.001$). The results of multivariate linear regression analysis showed that serum uric acid level did not have a significant effect on hand muscle strength, but it did have a significant effect on quadriceps muscle strength, both overall ($p=0.021$) and in elderly women ($p=0.001$).

Conclusion: The results of this study showed that with increasing serum uric acid levels, hand and quadriceps muscle strength increases, although in the adjusted model, this positive effect was present only on quadriceps muscle strength in elderly women.

Keywords: *Uric Acid, Hand Muscle Strength, Quadriceps Muscle Strength, Aging.*

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Introduction

With advancing age, muscle mass and strength decrease, resulting in impaired ability to perform activities of daily living, an increased risk of falls and fractures, and ultimately patient dependency (1, 2). Oxidative stress, chronic inflammation, and mitochondrial dysfunction have been shown to play important roles in age-related muscle atrophy (3). Oxidative stress is defined as an imbalance between oxidant and antioxidant levels (4). Considering the role of oxidative stress in muscle atrophy, it can be hypothesized that substances with antioxidant properties may exert a protective role in preventing the decline of muscle strength and mass (5). Uric acid is recognized as a strong antioxidant (6) and is responsible for two-thirds of the total antioxidant capacity of plasma (7).

In recent years, numerous studies have been conducted on the role of uric acid in muscle strength, although most of these studies have focused on hand muscle strength. However, quadriceps muscle strength is a more important predictor of functional performance in the elderly (8). Some of these studies have reported a positive association between uric acid levels and muscle strength (9-12). In the study by Kawamoto et al., a positive and protective role of serum uric acid levels on muscle strength was observed in an elderly female population (10). Additionally, in a historical cohort study by Huang et al., it was shown that in an elderly female population, uric acid has a protective effect against the decline of muscle strength (13). However, the results of some other studies have been different (14-16). In the study by Yi et al., it was observed that elderly individuals with hyperuricemia had poorer performance in muscle strength assessment tests (14). In the study by Chen et al., conducted on a middle-aged and elderly Chinese male and female population, hyperuricemia was associated with low skeletal muscle mass (15).

Considering the importance of muscle strength in the quality of life of the elderly, the contradictory results of previous studies, and the use of a superior indicator—quadriceps muscle strength alongside hand muscle strength—the present study was conducted with the aim of determining the relationship between serum uric acid levels and muscle strength in the elderly, using data from the Elderly Cohort Project in northern Iran.

Methods

This cross-sectional study is part of the second phase of the Amirkola Elderly Cohort Study (17), which was conducted following approval by the Ethics Committee of Babol University of Medical Sciences under code IR.MUBABOL.HRI.REC.1401.048. The sample size was estimated at approximately 800 participants, with a 95% confidence level, 80% power, and assuming r=0.10, based on the formula below; participants were enrolled through simple random sampling.

Formula for the confidence interval of the correlation coefficient: $\omega = \frac{1}{2} Ln \frac{1+r}{1-r}$

Sample size determination formula: $n = \frac{(z_{1-\frac{\alpha}{2}} + z_{1-\beta})^2}{\omega^2} + 3$

Individuals with incomplete records, those currently taking uric acid-lowering medications, and individuals with renal insufficiency were excluded from the study. Demographic information, including sex, age, and smoking history, was collected using a questionnaire. Anthropometric indices, including height (in centimeters) measured by a standing stadiometer and weight (in kilograms) measured by a Seca digital scale with minimal clothing and without shoes, were recorded. Body mass index (BMI) was calculated based on the formula: weight (in kilograms) divided by height (in meters) squared. Estimated glomerular filtration rate (eGFR) was calculated using the formula: (140 − age) × weight (in kilograms) / creatinine × 72 (× 0.85

if female) (18). The level of physical activity in the elderly was collected using the standard Physical Activity Scale for the Elderly (PASE) questionnaire (19). This questionnaire consists of three sections. The first section pertains to leisure-time activity and contains six questions. The second section contains three questions and pertains to household activity, and the third section pertains to work-related activity and includes one question. The score of this questionnaire ranges from zero to 400 or more, with higher scores indicating greater physical activity. The validity and reliability of the Persian version of this questionnaire were determined in the study by Keikavoosi-Arani et al. (20).

The diagnosis of diabetes was based on self-report and observation of a physician's prescription, or having two fasting blood glucose measurements equal to or greater than 126 (21). Additionally, in this study, hypertension was defined based on a mean systolic blood pressure greater than or equal to 140, or a diastolic blood pressure greater than or equal to 90, in the supine position (22).

A digital hand dynamometer manufactured in South Korea, which measures hand muscle force in kilograms, was used to assess hand grip strength. Quadriceps muscle strength was measured using a handheld dynamometer, which was secured on one side by a band above the ankle and on the other side by a spring scale attached beneath the chair, in kilograms. The participant sat in an upright position with their legs hanging in front of the chair. The participant was then asked to raise their legs at a 90-degree angle, parallel to the ground. This test was performed twice, alternating between the legs, with a 2-minute rest between each trial, and the maximum force applied was recorded in kilograms. The mean of the two upper or lower limbs was then calculated as the hand or quadriceps muscle strength.

Serum uric acid levels were measured using an autoanalyzer with Uricase and a reagent from Pars Azmoon Company, in milligrams per deciliter. Participants were then divided into four quartiles based on serum uric acid levels, and muscle strength was compared across these groups. Data were analyzed using SPSS version 22 and statistical tests including Pearson's correlation coefficient to examine the relationship between quantitative variables, analysis of variance (ANOVA) to compare the mean hand and quadriceps muscle strength according to serum uric acid levels, and multiple linear regression to control for variables affecting hand and quadriceps muscle strength; $p<0.05$ was considered significant.

Results

Of the 800 elderly individuals studied, 448 (56%) were male and 352 (44%) were female. The mean age of the study participants was 69.74±7.14 years, mean weight was 69.28±12.54 kg, mean height was 157.26±8.61 cm, mean BMI was 28.04±4.78, mean right arm muscle strength was 22.50±8.93 and left arm was 22.97±10.66, mean right quadriceps muscle strength was 19.71±10.68 and left was 20.06±10.64, mean creatinine was 1.03±0.25, mean uric acid was 4.99±1.71, and mean GFR was 69.94±22.80. In this study, with increasing serum uric acid levels, the mean hand muscle strength ($p=0.002$) and quadriceps muscle strength ($p=0.001$) increased significantly. Additionally, the variables of age, weight, height, BMI, creatinine, and hemoglobin were also significantly higher at higher uric acid levels; however, the mean eGFR decreased significantly with increasing uric acid levels (Table 1).

In the present study, a positive and statistically significant correlation was observed between serum uric acid levels and hand muscle strength ($r=0.134$, $p<0.001$), as well as quadriceps muscle strength ($r=0.161$, $p<0.001$) (Figure 1). To predict the role of variables influencing hand and quadriceps muscle strength, a multiple linear regression model was used. The variables of serum uric acid level, sex, age, smoking history, hypertension, diabetes, and physical activity were entered into the model as predictor variables. The variables of sex, age, and physical activity were the most important variables influencing changes in hand muscle strength in the elderly (Table 2). The results of regression analysis by sex showed that age and the

PASE questionnaire score were able to significantly predict changes in hand muscle strength in elderly men. Additionally, the variables of age, BMI, and diabetes were able to significantly predict changes in hand muscle strength in elderly women (Table 2). The variables of age, sex, and serum uric acid level were able to significantly predict changes in quadriceps muscle strength in the elderly (Table 3). Furthermore, regression analysis by sex showed that the variables of age and BMI in elderly men had a significant effect on quadriceps muscle strength, and in elderly women, the variables of age and serum uric acid level had a significant effect on quadriceps muscle strength (Table 3).

Table 1. Mean values of hand and quadriceps muscle strength and some quantitative variables studied according to different uric acid levels in the elderly of Amirkola

Variable	Uric acid level				p-value
	0-3.80 (n=203) Mean±SD	3.81-4.80 (n=203) Mean±SD	4.81-5.90 (n=205) Mean±SD	≥5.91 (n=189) Mean±SD	
Age	70.13±7.06	69.40±6.97	68.69±6.98	70.86±7.43	0.017
Weight	65.50±11.88	68.03±11.83	71.70±12.30	72.69±13.08	<0.001
Height	155.28±8.80	156.80±8.56	158.08±8.28	158.94±8.43	<0.001
BMI	27.20±4.63	28.67±4.38	28.57±5.26	28.75±4.64	0.003
Creatinine	0.92±0.21	1.00±0.21	1.05±0.23	1.13±0.29	<0.001
Hemoglobin	13.30±1.69	13.47±1.42	13.70±2.665	13.69±1.54	0.118
Hand strength	20.75±9.54	22.55±8.83	23.50±8.86	24.06±8.74	0.002
Quadriceps strength	17.77±9.05	19.33±9.59	20.22±9.66	22.42±12.61	<0.001
GFR	72.37±22.44	70.05±21.65	70.50±22.31	66.62±24.67	0.093
PASE score	96.98±54.29	103.44±56.31	102.37±62.34	96.96±55.66	0.537

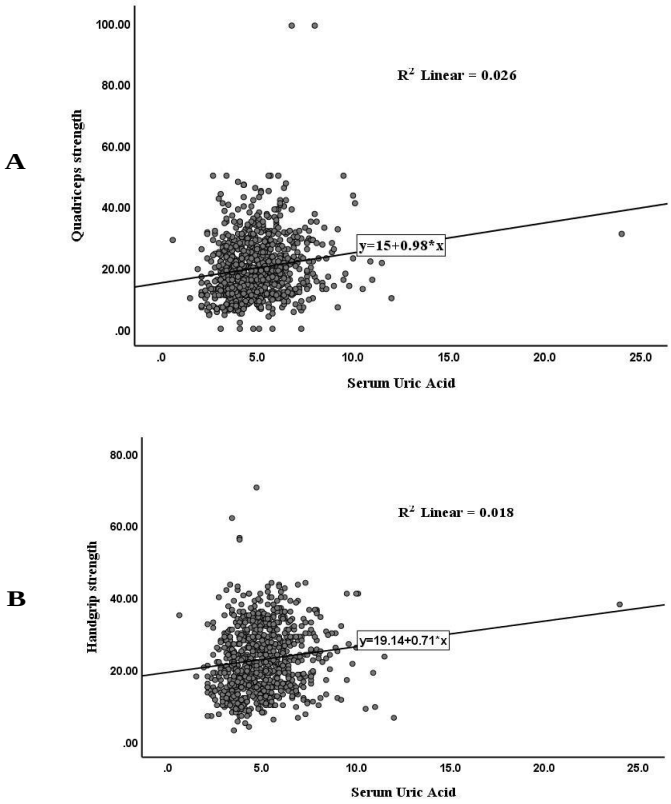


Figure 1. Scatter plot showing the relationship between serum uric acid levels and quadriceps muscle strength (A) and hand muscle strength (B) in the elderly population of Amirkola

Table 2. Multiple linear regression analysis for the prediction of hand muscle strength in the elderly population of Amirkola

Variable	Total			Men			Women		
	Unstandardized B	Standardized B	p	Unstandardized B	Standardized B	p	Unstandardized B	Standardized B	p
Serum uric acid level	0.22	0.04	0.113	0.17	0.04	0.353	0.23	0.06	0.252
Age	-0.38	-0.30	<0.001	-0.40	-0.39	<0.001	-0.37	-0.41	<0.001
Hypertension	-0.09	-0.01	0.866	-0.52	-0.03	0.465	0.31	0.02	0.669
Diabetes	-0.64	-0.03	0.197	-0.11	-0.01	0.889	-1.24	-0.09	0.047
BMI	-0.01	-0.01	0.830	0.14	0.08	0.089	-0.14	-0.12	0.031
PASE questionnaire score	0.01	0.08	0.004	0.02	0.12	0.007	0.01	0.05	0.392
Smoking history	0.53	0.02	0.440	0.59	0.03	0.433	0.65	0.01	0.908
Sex (male-to-female ratio)	11.81	0.65	<0.001	-	-	-	-	-	-

Table 3. Multiple linear regression analysis for the prediction of quadriceps muscle strength in the elderly population of Amirkola

Variable	Total			Men			Women		
	Unstandardized B	Standardized B	p	Unstandardized B	Standardized B	p	Unstandardized B	Standardized B	p
Serum uric acid level	0.42	0.07	0.021	0.20	0.04	0.427	0.84	0.17	0.001
Age	-0.37	-0.26	<0.001	-0.44	-0.33	<0.001	-0.28	-0.25	<0.001
Hypertension	0.45	0.02	0.516	0.95	0.05	0.338	-0.57	-0.03	0.539
Diabetes	-0.99	-0.04	0.137	-1.94	-0.09	0.064	0.040	0.003	0.960
BMI	0.10	0.05	0.147	0.26	0.11	0.021	-0.03	-0.02	0.70
PASE questionnaire score	0.002	0.013	0.683	0.001	0.009	0.847	0.002	0.014	0.797
Smoking history	-1.31	-0.05	0.154	-1.39	-0.06	0.177	1.21	0.01	0.867
Sex (male-to-female ratio)	11.61	0.56	<0.001	-	-	-	-	-	-

Discussion

Our findings showed that hand and quadriceps muscle strength had a direct and significant correlation with serum uric acid levels, and with increasing serum uric acid levels, hand and quadriceps muscle strength also increased. It was also observed that the mean hand and quadriceps muscle strength was significantly higher in the upper quartiles of serum uric acid; however, in the adjusted model, serum uric acid level was able to significantly predict only changes in quadriceps muscle strength, both overall and in women.

In the study by Kawamoto et al. (10), as in our study, the mean hand muscle strength was significantly higher at higher uric acid levels. In the study by Nahas et al. (11), as in our study, the mean quadriceps muscle strength showed an increase with increasing uric acid levels. Additionally, in the study by Molino-Lova et al., higher uric acid levels were associated with better muscle performance in elderly individuals (23). The results of some other studies were contrary to the results of our study. In the study by Chen et al. on middle-aged Chinese individuals, it was shown that hyperuricemia was independently associated with reduced skeletal muscle mass in both sexes (15).

In the study by Huang et al. (16), hand and quadriceps muscle strength was significantly lower in individuals with hyperuricemia, which may be due to the age difference between the two studies, as the mean age in the latter study was 45 years, whereas in our study it was 69.74 years. The precise mechanism by which uric acid increases muscle strength in elderly individuals is not known. One possible reason may be its antioxidant properties (7). Uric acid can act as an effective antioxidant, protecting muscles against free radicals and oxidative agents; consequently, the higher the serum uric acid level in elderly individuals, the greater its antioxidant effect, which may lead to improved muscle strength and function.

In our study, there was a positive relationship between serum uric acid levels and quadriceps muscle strength in women, which can be related to hormonal differences. Estrogen appears to enhance uric acid secretion and lead to increased uric acid levels in postmenopausal women (24), which may partially strengthen the notable association between uric acid and skeletal muscle mass in the overall female population. Additionally, with advancing age, testosterone levels decrease, which causes reduced muscle mass and strength in elderly men (25).

The limitations of this study include the following: the lack of measurement of oxidative stress biomarkers to justify the antioxidant effect of uric acid on muscle strength; the cross-sectional nature of the study, which makes it difficult to establish causal relationships; the absence of assessment of nutritional status and medications affecting serum uric acid levels as confounding variables; the restriction of the study to individuals over 60 years of age, which makes generalization of the results to other groups difficult; and our analysis, which was based on serum uric acid levels that reflect only a portion of the actual amount of uric acid stored in peripheral tissues. The strengths of this study include the large sample size, the population-based nature of the study, and the measurement of quadriceps muscle strength in addition to handgrip strength in both sexes.

The results of this study indicate that in the crude model, with increasing serum uric acid levels, hand and quadriceps muscle strength also increase; however, in the adjusted model, increased serum uric acid levels were associated only with increased quadriceps muscle strength in elderly women.

Conflicts of Interest: The authors of this article declare no conflicts of interest.

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