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Investigating the relationship between serum calcium and alkaline phosphatase with bone mineral density in active and inactive men

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Abstract
Purpose: Osteoporosis is a decrease in bone density among older adults that can cause painful fractures and disability. One of the most important effective non-pharmacological interventions is having appropriate and continuous physical activity. The aim of this study was to investigate the relationship between serum calcium and alkaline phosphatase with femur bone mineral density in active and inactive men. **Method:** This study was semi-experimental. 35 active and 35 inactive elderly men aged 65 to 80 years with medical records were selected. Anthropometric characteristics, serum calcium and alkaline phosphatase of subjects were used as effective indicators of osteoporosis. Pearson's correlation coefficient was used to find the relationship between femur mineral density and serum calcium and alkaline phosphatase, data analysis was done using SPSS version 26 Software. **Results:** The results of this research showed that in both groups of active and inactive men, there was a significant relationship between serum calcium and alkaline phosphatase and femur mineral density ($P \leq 0.05$). No significant relationship was found between the height index and mineral density of the femur ($P \geq 0.05$). **Conclusions:** In general, the results show that there is a significant relationship between bone density and weight, age, calcium, phosphorus, and serum alkaline phosphatase of all subjects, and the effect of exercise on other bone density indicators can be investigated.

Keywords: bone mineral density, calcium, alkaline phosphatase, active, men.

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INTRODUCTION

Osteoporosis is a common disease that causes bones to become thin and fragile, and usually a person develops this disease after middle age (Rinonapoli et al., 2021). This disease starts at a young age and progresses slowly over time. Early diagnosis of osteoporosis is very important and plays an effective role in raising the level of health and public health in the society (Bouvard, Annweiler, & Legrand, 2021). Based on the available reports, the prevalence of osteoporosis varies between countries and even within countries, differences in race, nutritional status, physical activity, and lifestyle are among the causes of these differences (Thambiah & Yeap, 2020). The World Health Organization committee uses bone mineral content (BMD) and T-Score to classify individuals into three conditions: healthy, osteoporosis, and osteoporotic. This definition is a practical technical definition in which an individual's bone mineral content (BMD) is compared to the mean maximum bone mass of a normal adult population. Today, osteoporosis is considered a great threat in the world and its annual mortality is more than all types of cancer (Cowdery et al., 2020). Age, weight, body mass index, gender, menopause, history of fractures, history of osteoporosis in first-degree relatives, nutritional factors, insufficient intake of calcium and vitamin D, inactivity and inactivity can be mentioned among the risk factors affecting osteoporosis (SHarMa et al., 2021). The findings showed that women have 5 times more primary fractures than men, but the risk of fractures within three years after the first fracture is relatively lower. Age is also effective in increasing the risk of osteoporosis, and the older you get, the more the incidence of osteoporosis increases. According to the statistics of the World Health Organization, the prevalence of hip fracture increases in people over 65 years of age, mostly after normal falls and due to minor injuries (Turk et al., 2020). Also, with age, the level of hormones (testosterone in men and estrogen in women) decreases and reduces bone density and makes bones more fragile (Zanker & Duque, 2019). It is known that the content of bone minerals increases during childhood and reaches its maximum during

puberty. After the third decade of life, the overall decrease in bone density begins and this decrease accelerates with age. Bone strength is due to the decrease in bone density decreases, and also the removal of bone is more than its repair, these cases make the chronological age to be considered as one of the main risk factors for the prevalence of osteoporosis (Marin, Pedrosa, Moreira-Pfrimer, Matsudo, & Lazaretti-Castro, 2010). On the other hand, bone is the main source of calcium and progenitor cells in the body. Among the various biological tests to estimate the activity of osteoblasts, it is important to measure the amount of alkaline phosphatase of the subject. Alkaline phosphatase is an coenzyme produced by osteoblast cells and performs the hydrolysis reaction of organic phosphates at alkaline ph. Calcium and phosphate are important components of inorganic bone matrix and are the main factors in maintaining bone health. In addition, studies have shown that the serum level of alkaline phosphatase ALP predicts the severity of bone loss (Alvarez-Pitti et al., 2020). Prevention and treatment of osteoporosis includes drug and non-drug interventions (Atlihan, Kirk, & Duque, 2021). Although the use of drugs such as bisphosphonates increases bone density and reduces the risk of fractures and falls in the elderly, so their treatment costs and side effects are worth considering. Meanwhile, non-drug treatments, especially proper sports activities, are less expensive than drugs and have no complications (Tibert et al., 2021). Decreasing physical activity and lack of sufficient movement during life significantly reduces bone minerals, in addition, intense sports activity significantly increases bone mineral density (Cavedon et al., 2020). Regular exercise during childhood and adolescence is considered to maintain health and personal hygiene during middle age and old age (Alvarez-Pitti et al., 2020). The findings of various studies also show that physical activity along with adequate intake of calcium and vitamin D has a great effect in reducing the speed of bone density loss. In fact, one of the effective, safe and cheap methods for preventing or delaying the occurrence of osteoporosis is regular exercise in a special way (Delkash & Farsad, 2020). Regular physical activity not only makes the bones healthy, but also has a direct effect on the overall health of the body by increasing muscle strength, creating balance and coordination in the body (Ilacqua, Emerenziani, Aversa, Guidetti, & Baldari, 2020). Exercises are recommended as a non-pharmacological intervention to increase bone

density in youth and prevent bone mass loss in middle-aged and old age. In elderly people, doing sports also plays an important role in increasing bone density, preventing falls and possible fractures (Pinheiro et al., 2020). Also, in various studies, the effect of physical activity in the prevention of bone tissue analysis has been mentioned, and considering that 40-44% of the bone density of an adult is achieved during adolescence, the effect of physical activity, especially during growth and has shown puberty on bone density (Iwamoto, 2017). Sports activity is a factor that maintains and stimulates the formation of bones, which leads to a reduction in the risk of bone fractures through the accumulation of minerals, strengthening muscles and improving the balance of a person (Espinosa et al., 2018). The effect of physical activity and the resulting mechanical pressure on increasing bone density has been proven; the mechanical pressure applied to the bone through tendons and muscles has a direct effect on bone formation and its deformation (Tong et al., 2019). Physical activities with two methods of muscle stretching and gravity. They cause the transfer of force to the bones: and they can increase bone density, so that people with active lives have significantly more bone mass than inactive people of the same age, and this benefit is maintained until the seventh and even eighth decades of their lives becomes (Holubiac & Grosu, 2019). Therefore, the aim of this study was to investigate the relationship between serum calcium and alkaline phosphatase with femur mineral density in active and inactive men.

METHOD

This study was semi-experimental. The statistical population of the current study consisted of all Iranian patients referred to Imam Hussein Malayer Hospital in the year 1401 A.S. in the age range of 65 to 80 years. The clinical information used in this study was related to 235 patients who had medical records in Imam Hussein Malayer Hospital during the years 1391-1401 due to osteoporosis. Of these, 85 men were randomly selected. After completing the questionnaire containing laboratory information of osteoporosis, anthropometric characteristics and physical activity level, 35 active elderly men and 35 inactive elderly men participated in this study. The sample size was estimated using the sample size estimation formula based on J-Power, taking into account the first type error of 0.05, the confidence coefficient of 95% and the test

power of 80%. Body mass index was obtained by dividing the person's weight in kilograms by the second power of height in meters. In this research, the subjects of the inactive group were people who did not do any specific sports activities and were similar in age to the active group. And the subjects of the active group included elderly men who had regular physical activity three sessions a week for at least one year. Lack of dietary control was one of the weak points of this study. Inclusion criteria included: male gender, age between 65 and 80 years, having medical records and clinical tests in the hospital and available via phone or internet. Exclusion criteria included: being treated for osteoporosis, history of taking hormonal drugs and having a chronic disease. After filling the consent form by the subjects, the information related to blood test and bone mineral density test was used. In the above study, the subjects' anthropometric characteristics (age, weight, height, body mass index) and serum parameters (calcium, vitamin D, phosphorus and alkaline phosphatase) were used. In the early hours of the morning, in the fasting state, blood samples of 5 ml each were taken from the subjects' brachial (anticubital) veins, so that all the blood samples were poured into tubes containing heparin anticoagulant immediately after blood collection and kept for 15 minutes. They were centrifuged at 3000 rpm. Then, Iranian Pars Azmoun kits with a sensitivity of one and five units per liter and Biochemistry 240 GLOBAL auto analyzer manufactured by PBC, Italy were used to measure the desired serum parameters. The body mass index was obtained by dividing the person's weight in kilograms by the second power of height in meters. In addition to descriptive statistics, Pearson's correlation coefficient test was used to analyze the research data. SPSS version 26 software was used for data analysis.

RESULTS

Table 1 shows the descriptive and anthropometric information of the subjects.

Table 1: Anthropometric information of subjects.

Variables	mean and standard	
	Active elderly men (n=35)	Inactive elderly men (n=35)
Age (years)	74.36 ± 8.45	75.34 ± 8.67
Height (cm)	166.67 ± 7.56	165.87 ± 7.53

weight (kg)	70.83 ± 12.68	71.55 ± 11.45

The values related to the correlation coefficient between serum calcium and alkaline phosphatase and femur mineral density of active and inactive men are shown in Tables 2 and 3, respectively. According to the data in Tables 2 and 3, it can be seen that in active and inactive men, a significant relationship was observed between anthropometric characteristics (age, weight) and serum indices (calcium and alkaline phosphatase levels) with femur mineral density ($P \geq 0.05$). While there was no significant relationship between other indices (height) and bone mineral density ($P \leq 0.05$).

Table 2. Correlation coefficient between osteoporosis indices and femur bone mineral density of active elderly men

Variables	**Osteoporosis indices of bone mineral density (BMD) in the active group (n=35)**	
	Correlation coefficient (r)*	significance level (p-value)
Age (years)	-0.76	0.047*
Height (cm)	-0.32	0.37
weight (kg)	0.75	0.022*
Serum calcium level	0.88	0.047*
serum alkaline phosphatase	-0.83	0.026*

• Significant difference at $P \leq 0.05$ level, *Pearson correlation coefficient

Table 3. Correlation coefficient between osteoporosis indices and femur bone mineral density of inactive elderly men

Variables	**Osteoporosis indices of bone mineral density (BMD) in the inactive group (n=35)**	
	Correlation coefficient (r)*	significance level (p-value)
Age (years)	-0.85	0.034*
Height (cm)	-0.21	0.47
weight (kg)	0.74	0.013*
Serum calcium level	0.87	0.027*

serum alkaline phosphatase	-0.76	0.037*

• Significant difference at P≤0.05 level, *Pearson correlation coefficient

DISCUSSION

The aim of this study was to investigate the relationship between serum calcium and alkaline phosphatase with femur bone mineral density in active and inactive men. The results showed that there is a significant relationship between age, weight, serum calcium and phosphorus levels and bone mineral content in active and inactive elderly men.

These results are consistent with most previous studies, especially in elderly men, showing that high weight is associated with higher BMD. Carvalho et al. (2019) reported that there is a positive and significant relationship between bone mineral density and body weight, so that higher mineral density values were reported in subjects who had more weight (Crispim Carvalho et al., 2019). Also, at the end of their study, Siring Liar et al. (2020) reported a strong correlation between mineral density and body weight, especially in the region of the spine and femoral neck, which bear mechanical pressure (Cirnigliaro et al., 2020). In contrast, a hospital study conducted in elderly men reported that obese and overweight men were more prone to osteoporosis and osteopenia, which was inconsistent with the results of the above study (Paniagua, Malphurs, & Samos, 2006). The possible explanation for the difference between these results may be related to the age of the subjects, research design, sampling method and methodological difference. The mechanisms by which body weight exerts positive effects on BMD status are not fully understood. The possible mechanism is related to the absorption of more force by the bones, the higher the body weight, the more force is applied to the bones and the bone density increases (Hashimoto, Shikuma, Mandai, Adachi, & Uchida, 2021). Also, the results of this study showed that there is a significant relationship between serum calcium, phosphorus and alkaline phosphatase with bone minerals in both active and inactive groups. Common markers of osteoporosis include calcium, phosphorus, and alkaline phosphatase, which are measured in the blood. Biochemical markers of bone resorption are said to be related to existing bone mass and help predict future bone loss (Saha et al., 2017). Many studies have been conducted to evaluate markers of bone resorption to predict bone loss and to

evaluate the correlation of markers with bone mineral density. In line with the above study, Hashimoto et al. (2021) reported a significant relationship between serum phosphorus and calcium levels with osteoporosis. In their study, Suzuki et al. (2018) found that adding vitamin D and calcium during treatment over a four-year period significantly improved lumbar bone mineral density in Japanese osteoporosis patients (Suzuki, Nakamura, & Kato, 2018). Jafari et al. (2019) reported a significant relationship between serum calcium and phosphorus with bone minerals, in their study, the relationship between body mass index and serum calcium and phosphate levels investigated diabetes and metabolic syndrome (Jafari-Giv et al., 2019). Contrary to the above study, Tariq et al. (2019), in a study titled "Alkaline phosphatase as a predictor of bone mineral density in the elderly" showed that alkaline phosphatase and bone calcium are not predictors of bone mineral density in the elderly with osteoporosis, while that alkaline phosphatase and serum calcium are strong predictors for healthy elderly people (Tariq, Tariq, Lone, & Khaliq, 2019). In this case, it seems that various factors such as the age, gender of the subjects, as well as environmental factors can answer the diversity of the results related to the density of these indicators. Source.

According to our findings, it seems that doing sports exercises both in the treatment and prevention of osteoporosis has a positive effect in maintaining bone mass and preventing fractures and falls throughout life. Studies show that the density of bone mass of people who have more physical activity throughout their life is higher than their inactive peers (Marini et al., 2020). A common theory considers the bone as a piezoelectric crystal in which the mechanical pressure is converted into electrical energy, and electrical changes occur, and when the bone is subjected to mechanical pressure, the activity of the building cells stimulates the bone, and The result is the formation of calcium, which probably in postmenopausal women, the bone-forming cells/osteoblasts of different parts of the body, including the hands, trunk, and legs, are less stimulated, and as a result, calcium absorption is less, and therefore causes no changes in the density and content of bone minerals in the upper and lower limbs. In line with recovery and reconstruction, bone increases. Also, various clinical trials have shown that high-intensity

stretching exercises are effective on bone mass density, therefore, today, as a part of the treatment protocol for osteoporosis; exercise is recommended (Sjöblom et al., 2020). In line with the results of the present study, Rahimi et al. (2020) evaluated the effect of exercise on the bone density of the neck, femur, and lumbar vertebrae of the elderly. Their findings showed that in the group that exercised, bone mineral density in the region of the neck of the femur and lumbar vertebrae increased by 1%, while in the control group, a 2% decrease in bone density was observed (Mohammad Rahimi et al., 2020). In a study in which Kemmler et al. (2007) measured the long-term effect of physical exercises (stretching, strength and high-intensity aerobic exercises) on the bone mineral density of the lumbar vertebrae and pelvis, they observed that the bone mineral density in the active group compared to the inactive group has increased and the rate of bone mass loss has been slower (Kemmler et al., 2007). In a study by Yu et al. (2019) they investigated the effect of a 24-week period of aerobic exercise on the bone density of the elderly.

The mineral density of the femur and lumbar vertebrae increased in the active group and decreased by 1% in the control group (Yu et al., 2019). One of the limitations of the present research was the impossibility of determining the role of the diet used by the subjects in the past years due to the importance of diet in the bone density of people. Another limitation was the lack of available medical records of subject's aged 70 to 85, especially active people. The more the number of subjects, the more accurate and complete results of the relationship between blood factors and anthropometry and bone density can be obtained and can be used to identify people with osteoporosis. Therefore, it is suggested to use the above indicators in the process of checking the level of osteoporosis. Finally, considering the positive effect of exercise and the uncomplicated nature of most exercise, it is suggested that elderly people follow a regular exercise program after consulting with sports medicine specialists.

CONCLUSIONS

In general, it can be said that one of the applications of the results of this research is the use of body mass index and the serum amount of calcium and alkaline phosphatase indices in predicting the bone density of people.

Also, it is possible to use these serum and anthropometric variables to identify people with osteoporosis during adulthood and old age.

Conflict of Interests

The authors declare that they have no conflict of interests to disclose.

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