



## Research Article

## Evaluation of the Relationship between Osteoporosis and Body Fat Mass of the Upper and Lower Extremities by Dual-Energy X-Ray Absorptiometry

Numan Salman Dawood<sup>1\*</sup> , Zainab Sami Abdel Aziz<sup>2,3</sup>, Haneen Maan Alkhaales<sup>4</sup> 

<sup>1</sup> Department of Physiology, College of Medicine, University of Baghdad, Baghdad, Iraq; <sup>2</sup> Department of Internal Medicine, Al-Yarmouk Teaching Hospital, Baghdad, Iraq; <sup>3</sup> Department of Dentistry, AL Hikma University College, Baghdad, Iraq; <sup>4</sup> Furness General Hospital Dalton Lane, Barrow-In-Furness, Cumbria, LA14 4LF, UK

Received: 24 November 2023; Revised: 27 December 2023; Accepted: 30 December 2024

## Abstract

**Background:** Using dual-energy X-ray absorptiometry, body fat mass has been determined. The assessment of body fat mass was conducted utilizing dual-energy X-ray absorptiometry analysis of the pelvis and vertebral column. While it is acknowledged that osteoporosis can impact both body fat mass and bone mineral density, the particulars of this relationship currently remain uncertain. **Objective:** The aim of the present investigation is to assess gender differences in the effects of osteoporosis on the body fat mass of the upper and lower extremities. **Method:** 170 individuals participated (85 males and 85 females) in this study. Patients who presented with bone discomfort consisted of 40 males and 40 females. In addition, 90 apparently healthy volunteers, consisting of 45 males and 45 females, were studied and considered to constitute the control group. Dual-energy X-ray absorptiometry was utilized to determine the bone mineral density and body fat mass of every participant for all body parts. **Results:** Statistically significant disparities in body fat mass were observed between males and females, as well as between the control group and patients diagnosed with osteoporosis. **Conclusions:** Our results indicate that the patients with osteoporosis showed an increase in body fat mass (for both sexes). Other results obtained from this research revealed that females were more frequently suffering from osteoporosis than males.

**Keywords:** Body fat mass, Bone mineral density, Dual-energy X-ray absorptiometry scan, Osteoporosis, Upper and lower limbs.

تقييم العلاقة بين هشاشة العظام وكتلة الدهون في الجسم في الأطراف العلوية والسفلية عن طريق قياس امتصاص الأشعة السينية ثنائي الطاقة

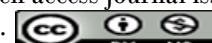
## الخلاصة

**الخلفية:** باستخدام قياس امتصاص الأشعة السينية المزدوج الطاقة، تم تحديد كتلة الدهون في الجسم. تم تقييم كتلة الدهون في الجسم باستخدام تحليل قياس امتصاص الأشعة السينية ثنائي الطاقة للحوض والعمود الفقري. في حين أنه من المسلم به أن هشاشة العظام يمكن أن تؤثر على كل من كتلة الدهون في الجسم وكثافة المعادن في العظام، إلا أن تفاصيل هذه العلاقة لا تزال غير مؤكدة حاليًا. **الهدف:** تقييم الفروق بين الجنسين في آثار هشاشة العظام على كتلة الدهون في الجسم في الأطراف العلوية والسفلية. **الطريقة:** شارك في هذه الدراسة 170 فرداً (85 ذكراً و85 أنثى). يتكون المرضى الذين يعانون من عدم الراحة في العظام من 40 ذكراً و40 أنثى. بالإضافة إلى ذلك، تمت دراسة 90 متطوعاً يتمتعون بصحة جيدة، يتألفون من 45 ذكراً و45 أنثى، وتم اعتبارهم يشكلون المجموعة الضابطة. تم استخدام قياس امتصاص الأشعة السينية ثنائي الطاقة لتحديد كثافة المعادن في العظام وكتلة الدهون في الجسم لكل مشارك لجميع أجزاء الجسم. **النتائج:** لوحظت فروق ذات دلالة إحصائية في كتلة الدهون في الجسم بين الذكور والإناث، وكذلك بين المجموعة الضابطة والمرضى الذين تم تشخيص إصابتهم بهشاشة العظام. **الاستنتاج:** أن المرضى الذين يعانون من هشاشة العظام أظهروا زيادة في كتلة الدهون في الجسم (لدى الجنسين). وكشفت النتائج الأخرى التي تم الحصول عليها من هذا البحث أن الإناث يعانين بشكل متكرر من هشاشة العظام أكثر من الذكور.

\* **Corresponding author:** Numan S. Dawood, Department of Physiology, College of Medicine, University of Baghdad, Baghdad, Iraq; Email: [numans@comed.uobaghdad.edu.iq](mailto:numans@comed.uobaghdad.edu.iq)

**Article citation:** Dawood NS, Abdel Aziz ZS, Alkhaales HM. Evaluation of the Relationship between Osteoporosis and Body Fat Mass of the Upper and Lower Extremities by Dual-Energy X-Ray Absorptiometry. *Al-Rafidain J Med Sci.* 2024;6(1):34-38. doi: <https://doi.org/10.54133/ajms.v6i1.410>

© 2024 The Author(s). Published by Al-Rafidain University College. This is an open access journal issued under the CC BY-NC-SA 4.0 license (<https://creativecommons.org/licenses/by-nc-sa/4.0/>).



## INTRODUCTION

A decrease in bone mineral density (BMD) is a hallmark of the common global disease osteoporosis. This decrease in bone mass and the associated modification of bone structure lead to heightened bone fragility and an elevated risk of fracture [1]. Bone mass is primarily influenced by BMD and is commonly utilized as a diagnostic marker for osteoporosis [2]. BMD is the most informative measure of bone quality that can be used in clinical management, where BMDs that are higher or lower than what is considered to be the normal range are strongly indicative of bone health problems [3]. Dual Energy X-Ray Absorptiometry (DEXA) is the best X-ray technique that can be used in scanning for and in the determination of BMD. It is characterized by its excellent spatial resolution, directionality, accuracy, and speed of implementation, with only very limited patient exposure to X-rays. A gamma camera is capable of detecting any actual bone issues [4,5]. Body fat mass (BFM) refers to the quantity of adipose tissue present in the human body. The body mass index (BMI) is considered a valuable factor in comparing body fat and body fat distribution in both sexes [6]. Specifically, research indicates that women tend to have a proportion of body fat that is approximately 10% greater than men [7,8]. Many studies have demonstrated that individuals with a lower body weight are more susceptible to fractures. Nevertheless, prior research has also demonstrated that the application of mechanical force, either body weight on the extremities or during exercise (in a suitable and regular way), will lead to an increase in BMD [7]. The above disparity in body fat between men and women arises due to the fact that women, at certain stages of their lives, may provide substance to a developing fetus and, subsequently, a newborn, through their own bodily resources [9,10]. Historically, studies have indicated that obesity and osteoporosis were independent conditions; however, current research has revealed a significant overlap in genetic and environmental factors between these two disorders [11]. Various studies have revealed that fat mass may potentially have positive impacts on bone health [12]. Nevertheless, there are conflicting findings, indicating that an increased fat mass will not necessarily provide a protective effect against osteoporosis or fracture [13]. Numerous studies have demonstrated a higher prevalence of osteoporosis in women compared to men, a difference that can be attributed to the anatomical, occupational, and hormonal differences between the two sexes [14]. The purpose of this work is to assess the relationship between body fat mass (BFM) and osteoporosis in the upper and lower extremities, including both sides of the body, in both healthy and osteoporotic individuals of both sexes.

## METHODS

### *Study design and setting*

The study was conducted from December 2022 to May 2023. The patients were chosen from the Rheumatology Outpatient Clinic at Baghdad Teaching Hospital, located in Medical City, Baghdad, Iraq. The study sample consisted of 170 volunteers of diverse genders and ages spanning from 20 to 45 years. The participants were classified into control and patient groups based on their gender, as outlined in Table 1.

**Table 1:** Classification of study participants into two categories

Total participants		Controls		Patients	
170		90		80	
Male	Female	Male	Female	Male	Female
85	85	45	45	40	40

### *Ethical considerations*

The study received ethical approval from the University of Baghdad, College of Medicine, in partnership with the Ministry of Health (specifically, the outpatient clinic of the Medical City Teaching Hospital). In addition, explicit agreement was sought from each participant.

### *Sample selection and inclusion criteria*

None of the study's participants had previously complained of hypertension or diabetes mellitus, were nonsmokers, and had not received any long-term medication in the four months preceding the study. In other words, with the exception of patients who attended the rheumatology out-clinic and complained of severe bone pain, the participants had not previously complained of any ailment, whereas the control group was otherwise healthy and had not complained of any such musculoskeletal concerns.

### *Outcome measurements*

All participants' weights and heights were recorded, as well as their DEXA scans. For all control and patient groups, the DEXA device was utilized to assess the bone mineral density (BMD) and body fat mass (BFM) of the full bodies of all participants, with special focus paid to evaluating the upper and lower extremities on both sides of the body.

### *Statistical analysis*

Statistical analyses were conducted using version 22 of the Statistical Package for Social Sciences (SPSS) software. Depending on the number of samples, paired and unpaired *t*-tests were used to analyze the differences between the control (normal) and osteoporosis groups. Means and standard errors were determined, and statistical significance assigned to a *p*-value less than 0.05.

## RESULTS

The anthropometric measurements of male and female subjects of varying ages (20 to 45 years) were collected: the mean age was  $38.85 \pm 1.99$  for males

and  $39.68 \pm 1.82$  for females; the mean height was  $172.85 \pm 1.19$  cm for males and  $166.75 \pm 1.12$  cm for females; and the mean weight was  $80.7 \pm 3.86$  kg for males and  $84.67 \pm 2.95$  kg for females, as shown in Table 2.

**Table 2:** The anthropometric measurements of the male and female subjects considered in this study

	Male	Female
Age (20-60 years old)	$52.85 \pm 1.99$	$48.68 \pm 1.82$
Height (cm)	$172.85 \pm 1.19$	$166.75 \pm 1.12$
Weight (kg)	$85.7 \pm 3.86$	$89.67 \pm 2.95$

Values were expressed as mean  $\pm$  SEM.

Table 3 lists the questionnaire responses, broken down by sex, for those who took part in the study. In spite of the fact that the DEXA scan was performed on the entire body, including the spine and hip, the reduction in BFM for the upper and lower limbs was recorded in the current study. These findings included the effects of osteoporosis (80 subjects), which were compared to the normal BFM of the 90 controls (healthy subjects) for these limbs.

**Table 3:** Summary of the responses to the questionnaire completed by the study participants

	Male	Female
Normal	45	45
Osteoporosis	40	40
Dominancy of arm and leg (routine and hard work)	Left side= 32 Right side= 53	Left side= 30 Right side= 55

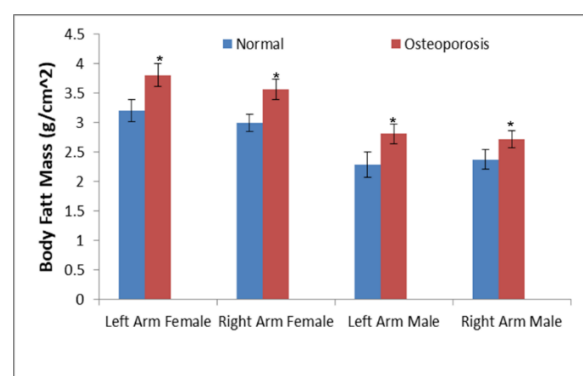
The means for the BFMs for the upper extremities (left and right arms) of the female and male participants in this study are reported in Table 4. Table 4 demonstrates that the mean BFMs in the upper limbs of females in the two groups considered (control and osteoporosis) are greater than those of males in the same groups and for the same side of the body. For females, the BFM in the right arm was less than for the left arm in the control group by 6.3%, while in the osteoporosis group, the right arm was less by 5.3%. In males, the BFM for the left arm was less than for the right arm by 3.3% for the control, while in the osteoporosis group it was greater by 3.4%. The BFM found for the left arm of females was greater than in the left arm of males in both groups, control and osteoporosis, by 23.5% and 22%, respectively; the BFM of the right arm in females, by contrast, was greater than that for males in both groups (control and osteoporosis) by 26% and 28%, respectively. Also, the BFMs found for the left and right arms of females in the osteoporosis group were greater than in the control group by 20.16% and 18.9%, respectively, whereas the BFMs for the left and right arms of males in the osteoporosis group were greater than those for the control group by 22.6% and 14.7%, respectively. Figure 1 shows that there are no significant differences between the mean BFM in the left and right arms of the control or osteoporosis cases for females; the same is true for males.

**Table 4:** The means for the BFMs for the left and right arms of the participants as categorized by sex

Organ	Normal	Osteoporosis	p-value
Left Arm Female	$3.198 \pm 0.145$	$3.801 \pm 0.172$	< 0.001
Right Arm Female	$2.995 \pm 0.182$	$3.559 \pm 0.196$	< 0.001
Left Arm Male	$2.289 \pm 0.215$	$2.807 \pm 0.166$	< 0.001
Right Arm Male	$2.368 \pm 0.165$	$2.715 \pm 0.145$	< 0.001

Values are expressed as mean  $\pm$  SEM. p-value represents the comparisons between normal and osteoporosis groups.

In addition, highly statistically significant differences ( $p < 0.001$ ) were found in the BFMs for the control and osteoporosis groups for the left arm in females; this also applies when comparing females' right arm. In the same way, there are highly statistically significant ( $p < 0.001$ ) differences in the BFMs of the control and osteoporosis groups for the left arm of males; this was also the case for males' right arms.



**Figure 1:** Comparison of the mean BFMs of the control and osteoporosis groups for the upper extremities for both sexes. \*significant differences compared to the normal subjects ( $p < 0.001$ ).

The mean BFMs for the lower extremities (left and right legs) of the female and male participants in this study are reported in Table 5.

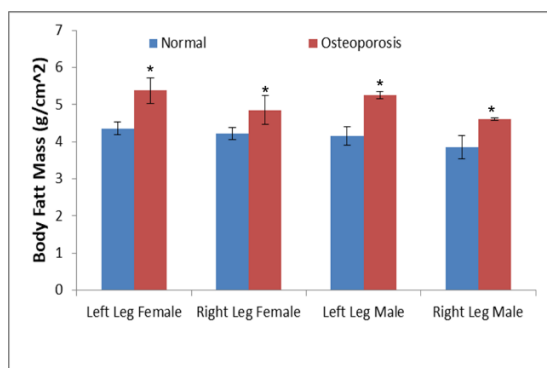
**Table 5:** The mean BFMs of the left and right legs for participants according to sex

Organ	Normal	Osteoporosis	p-value
Left Leg Female	$4.358 \pm 0.164$	$5.377 \pm 0.348$	< 0.001
Right Leg Female	$4.221 \pm 0.161$	$4.847 \pm 0.388$	< 0.001
Left Leg Male	$4.157 \pm 0.246$	$5.252 \pm 0.095$	< 0.001
Right Leg Male	$3.851 \pm 0.306$	$4.606 \pm 0.038$	< 0.001

Values are expressed as mean  $\pm$  SEM. p-value represents the comparisons between normal and osteoporosis groups.

Table 5 demonstrates that the mean BFMs in the lower limbs of females in each group (control and osteoporosis) are greater than those of males in the same groups and on the same side of the body. In females, the BFM for the left leg was greater than for the right leg in the control group by 3.3%, while in the osteoporosis group it was greater by 10.9%. For males, the BFM in the left leg was greater than in the right leg in the control group by 8%, while in the osteoporosis group it was greater by 14%. The BFM for the left leg in females was greater than in the left leg of males for the two groups (control and osteoporosis) by 4.9% and 2.4%, respectively; the same was true for the right leg by 9.6% and 5.23%,

respectively. Also, the BFM for the left and right legs of females in the osteoporosis group were greater than for the control group by 23.35% and 14.85%, respectively, whereas for males, these same figures were 26.34% and 19.6%, respectively. Figure 2 demonstrates that there are no significant differences between the mean BFM for the left and right legs of the control and osteoporosis groups in females; the same was also true for males. In addition, highly statistically significant differences ( $p < 0.001$ ) were found in the BFM of the control and osteoporosis groups in the left leg for females; the same was true of females' right legs. There were highly statistically significant ( $p < 0.001$ ) differences in the BFM of the control and osteoporosis groups for the left leg of males; the same was true for males' right legs.



**Figure 2:** Comparison of the mean BFM for the normal and osteoporosis groups for the lower extremities for both sexes. \*significant differences compared to the normal subjects ( $p < 0.001$ ).

## DISCUSSION

It is well known that osteoporosis is one of the most common disorders affecting the bone, where osteoporotic bone is fragile and easily fractured [15]. The best and safest diagnostic device to predict osteoporosis is the DEXA device [4]. DEXA is considered to be highly beneficial in measuring the mineral density, fat mass, and lean mass of each part of the body. Although considerable research has been undertaken to examine the relationship between BFM and BMD, the nature of this relationship, to date, remains obscure. One of the results of this study is that BFM, in general, was found to be greater in females in terms of the fat mass of the extremities. This is corroborated by the findings of Camhi *et al.* [16], who also found that the fat mass index of the extremities in females was much greater than that of males. The most crucial finding in this research was that BFM had a negative relationship with BMD in both the upper and lower extremities in both sexes; this result can clearly be seen in Tables 4 and 5. This finding agreed with various other similar studies [4,17,18]. This negative relationship between BFM and BMD is more apparent in females than in males. However, Jain and Vokes [17] concluded that males were more liable to fracture due to osteoporosis following an increase in BFM than females. However, the present study revealed contradictory

results, i.e., osteoporosis. The contrast between the results of the present study and those of Rejesh and Tamara could possibly be related to an occupational factor or genetic or environmental causes. Regarding the BFM of the upper limbs and, consequently, osteoporosis, the level was higher for the left side than the right. Since about 80% of the population have a right-handed dominance [19], and since exercise (normal, regular, and healthy exercise) will increase BMD [20], the right upper limb showed a reduction in BFM and so a relatively low degree of osteoporosis for males, while for females the opposite was true (i.e., higher BFM and so more osteoporosis of the right was seen than for the left upper extremities). This could possibly be explained by the fact that females tend to run the household, and even though they work, they do not undertake what would be considered healthy regular exercise. This suggests that housework is harmful (unhealthy) to bone health; Coupland *et al.* [21] offered similar findings and an explanation. Regarding the result for the lower limbs of both sexes, BFM was found to increase for osteoporotic subjects (see Table 5). The lower limbs revealed an increase in BFM on both sides for females to a greater extent than for males. This same result has been found in previous studies, which attributed an increase in fat mass/cm<sup>2</sup> to increased osteoporosis [17]. In this study, Table 2 shows females' weights were greater than those of males, and their heights were lower. The differences in BFM for the lower limbs of the control and osteoporotic groups on the same side were relatively small. In other words, the BFM of the right leg of females in the control and osteoporotic patients revealed little increase compared to the right leg of males; the same was observed for the left leg. This small difference between males and females can be explained by the fact that both sexes do considerably different amounts of exercise in terms of walking, running, and climbing stairs. This was in agreement with the results obtained by Benedetti *et al.* [22].

## Study limitations

In order to achieve more accurate and reliable results, the number of participants in this study should be increased. Additionally, it is preferable to categorize patients and controls by decade of age.

## Conclusion

Dual-energy X-ray absorptiometry scans of the whole body, or even just one part at a time, show good results when used as extra parameters instead of DXA scans that only look at the spine or hip. The findings of our study showed that individuals diagnosed with osteoporosis exhibited a relative increase in body fat mass, which was true for both sexes. Additionally, females were more frequently diagnosed with osteoporosis than males, although the right side was dominant in the upper limbs of both sexes. In addition, exercise adversely affects bone mineral density if done in the wrong way. Additional findings derived from this study indicate that

variations in the severity of osteoporosis between the lower and upper extremities, as well as between males and females, were more conspicuous in the lower limbs than the upper.

### Recommendation

Despite the small number of patients in each instance (control and osteoporosis), which was a drawback of this study in terms of further analysis, the results were promising. As a result, additional research involving a larger number of patients is required to facilitate a more comprehensive statistical analysis and, as a result, obtain more precise findings to substantiate the results of the current study and determine whether this methodology constitutes a reliable source of medical examination. Furthermore, it is crucial to compare the BFM of people with various disorders to that of healthy people and patients.

### ACKNOWLEDGMENTS

The authors thank the College of Medicine, University of Baghdad, and the staff of the Outpatient Rheumatology Clinic, Bone Mineral Density Unit (DEXA Unit), Baghdad Teaching Hospital, Medical City, Baghdad, for help and guidance during the study.

### Conflict of interests

No conflict of interests was declared by the authors.

### Funding source

The authors did not receive any source of fund.

### Data sharing statement

Supplementary data can be shared with the corresponding author upon reasonable request.

### REFERENCES

- Akkawi I, Zmerly H. Osteoporosis: Current concepts. *Joints*. 2018;6(2):122-127. doi: 10.1055/s-0038-1660790.
- Abdel Aziz ZS, Dawood NS, Al-khalisy MH. Evaluation of the effect of type II diabetes mellitus on bone mineral density of upper and lower limbs by dual-energy X-ray absorptiometry. *J Fac Med Baghdad*. 2023;65(1):27-33. doi: 10.32007/jfacmedbagdad.6511980.
- Kranioti EF, Bonicelli A, García-Donas JG. Bone-mineral density: clinical significance, methods of quantification and forensic applications. *Res Rep Forens Med Sci*. 2019;9(2):9-21. doi: 10.2147/RRFMS.S164933.
- Gonera-Furman A, Bolanowski M, Jędrzejuk D. Osteosarcopenia—The role of dual-energy X-ray absorptiometry (DXA) in diagnostics. *J Clin Med*. 2022;11(9):2522. doi: 10.3390/jcm11092522.
- Dawood NS, A method for source-depth estimation using a Hybrid Optical/Gamma Camera, in Physics Department. 2018, University of Leicester: Leicester, UK. Available at: <https://hdl.handle.net/2381/43791>
- Dawood NS, Musstaf RA, AL-Sahlane MHR. Model for prediction of the weight and height measurements of patients with disabilities for diagnosis and therapy. *Int J Bioautomation*, 2021;25(4):343–352. doi: 10.7546/ijba.2021.25.4.000824.
- Arif, M, Gaur DK, Gemini N, Iqbal ZA, Alghadir AH. Correlation of percentage body fat, waist circumference and

- waist-to-hip ratio with abdominal muscle strength. *Healthcare*. 2022;10(12):2467. doi: 10.3390/healthcare10122467.
- Kim DH, Lim H, Chang S, Kim JN, Roh YK, Choi MK. (2019). Association between body fat and bone mineral density in normal-weight middle-aged Koreans. *Korean J Fam Med*. 2019;40(2):100–105. doi: 10.4082/kjfm.17.0082.
- Ponti F, Santoro A, Mercatelli D, Gasperini C, Conte M, Martucci M, et al. Aging and imaging assessment of body composition: From fat to facts. *Front Endocrinol*. 2020;10(3):861-866. doi: 10.3389/fendo.2019.00861.
- Camhi SM, Bray GA, Bouchard C, Greenway FL, Johnson WD, Newton RL, et al. The relationship of waist circumference and BMI to visceral, subcutaneous, and total body fat: sex and race differences. *Obesity (Silver Spring)*. 2011;19:402–408. doi: 10.1038/oby.2010.248.
- Yanovski SZ, Yanovski JA. Toward precision approaches for the prevention and treatment of obesity. *JAMA*. 2018;319(3):223–224. doi: 10.1001/jama.2017.20051.
- Migliaccio S, Greco EA, Fornari R, Donini LM, Lenzi A. Is obesity in women protective against osteoporosis? *Diabetes Metab Syndr Obes Target Ther*. 2011;4:273–282. doi: 10.2147/DMSO.S11920.
- Alswat KA. Gender disparities in osteoporosis. *J Clin Med Res*. 2017;9(5):382–387. doi: 10.14740/jocmr2970w.
- Tornero-Aguilera JF, Villegas-Mora BE, Clemente-Suárez VJ. Differences in body composition analysis by DEXA, skinfold and BIA methods in young football players. *Children (Basel, Switzerland)*. 2022, 9(11):1643. doi: 10.3390/children9111643.
- Dimai HP. Use of dual-energy X-ray absorptiometry (DXA) for diagnosis and fracture risk assessment; WHO-criteria, T- and Z-scores, and reference databases. *Bone*. 2017;104:39–43. doi: 10.1016/j.bone.2016.12.016.
- Camhi SM, Bray GA, Bouchard C, Greenway FL, Johnson WD, Newton RL, et al. The relationship of waist circumference and BMI to visceral, subcutaneous, and total body fat: sex and race differences. *Obesity*. 2011;19(2):402–408. doi: 10.1038/oby.2010.248.
- Jain RK, Vokes T. Fat mass has negative effects on bone, especially in men: A cross-sectional analysis of NHANES 2011-2018. *J Clin Endocrinol Metab*. 2022;107(6):e2545–e2552. doi: 10.1210/clinem/dgac040.
- Zhao LJ, Jiang H, Papisian CJ, Maulik D, Drees B, Hamilton J, et al. Correlation of obesity and osteoporosis: effect of fat mass on the determination of osteoporosis. *J Bone Miner Res*. 2008;23(1):17-29. doi: 10.1359/jbmr.070813.
- Sergi G, Perissinotto E, Zucchetto M, Enzi G, Manzato E, Giannini S, et al. Upper limb bone mineral density and body composition measured by peripheral quantitative computed tomography in right-handed adults: the role of the dominance effect. *J Endocrinol Invest*. 2009;32(4):298-302. doi: 10.1007/BF03345715.
- Corballis MC. Left brain, right brain: facts and fantasies. *PLoS Biol*. 2014;12(1):e1001767. doi: 10.1371/journal.pbio.1001767.
- Coupland CA, Grainge MJ, Cliffe SJ, Hosking DJ, Chilvers CE. Occupational activity and bone mineral density in postmenopausal women in England. *Osteoporosis Int*. 2020;11(4):310–315. doi: 10.1007/s001980070119.
- Benedetti MG, Furlini G, Zati A, Letizia Mauro G. The effectiveness of physical exercise on bone density in osteoporotic patients. *Biomed Res Int*. 2018;4840531. doi: 10.1155/2018/4840531.