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Evaluation of the Effect of Type II Diabetes Mellitus on Bone Mineral Density of Upper and Lower Limbs by Dual-Energy X-Ray Absorptiometry

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Abstract

Background: Bone mineral density has been assessed using Dual-Energy X-Ray Absorptiometry. Bone mineral density is measured according to the results of the Dual-Energy X-Ray Absorptiometry examination of the vertebral column and pelvis. Although diabetes mellitus type II (DM) is known to affect bone mineral density, at the present time this particular relationship is not clear.

Objective: The aim of current study was to evaluate the effects of type II diabetes mellitus on bone mineral density of the upper and lower limbs as well as gender differences.

Methods: This study involved 165 patients complaining of bone pain (85 males and 80 females), 85 patients of who suffered from diabetes, involving both genders. In addition, 90 apparently healthy volunteers had been studied and were considered to constitute the control group. All individuals (255) were studied regarding their bone mineral density via Dual-Energy X-Ray Absorptiometry for all parts of the body.

Results: The Dual-Energy X-Ray Absorptiometry exam revealed highly statistically significant differences between the sides of the body in the same person. In addition, there were significant differences in bone mineral density between females and males, as well as between the control and patient groups with type II diabetes mellitus.

Conclusion: Our results indicated that the bone mineral density of women was less than that in men in all cases (normal, osteoporosis, and diabetes mellitus type II (DM) with osteoporosis). Other results obtained from this research revealed that diabetes mellitus type II (DM) can be considered to be one of the major causes of osteoporosis in the general population.

Keywords: Bone mineral density; Dual-Energy X-ray absorptiometry scan; Diabetes mellitus type II (DM); Osteoporosis; Upper and Lower limbs.

Introduction:

Bone mineral density (BMD), represents the most informative evaluation of bone quality that can be applied in clinical management. In addition, when it is higher or lower than the normal limits, this is an indication of health problems in bones (1). For example, a change in the BMD in the upper limbs (left and right arm) and lower limbs (left and right legs) of the human body leads to an increased risk of fracture. Bone mineral density scanning is an improved form of the X-ray technique, which can develop spatial resolution and directional accuracy, can be rapidly implemented, and results in very limited exposure to radiation due to the short time required for Dual-Energy X-Ray Absorptiometry (DEXA) which makes this technique more effective than previous ones (2). In order to perform the BMD evaluation, the attenuation properties of various materials within the body are calculated in relation to the photon energy. There are many potential sites for the examination; however, the lumbar spine, the hip, and the femur tend to be the most common choices. A scan of the whole body is typically carried out as well (3). The greatest benefit of the measurement is that it is expressed as an absolute value of a BMD (g/cm^2), which permits direct comparison with prior scans to evaluate a patient's health history based on age and gender (4). In addition, DEXA scans can evaluate body components and differentiate between lean and fat mass based on the different attenuation properties of different tissues. This enables monitoring the health condition of bones (5). For the diagnosis of osteopenia and osteoporosis via DEXA scan, the World Health Organization (WHO) determined the appropriate threshold values in 1994. These thresholds represent the gold standard for the clinical diagnosis of osteoporosis, with the DEXA scan subsequently emerging as the best form of examination in the field of bone densitometry. In particular, according to the T-score, the WHO classifies bone mineral density as normal when it is in the range 1 to -1.0, as osteopenia when it is between -1.0 and -2.5, as osteoporosis when it is below -2.5, and as severe osteoporosis when it is a considerably below -2.5 and fragility fractures are apparent (6,7). Diabetes mellitus (DM) is a chronic disease that affects the whole body and can lead to a wide variety

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of complications, including cardiovascular disease, neuropathy, and osteoporosis (8). Type I diabetes mullitus and Type II diabetes mellitus, despite having quite distinct underlying mechanisms, both contribute to an increased risk of fracture, which is caused by a number of factors and can be partially explained by loss of BMD (9). The most common effect is the danger of hip or spine fracture, which is approximately 2.4 - 7 times greater in DM I and approximately 2-3 times more in DMII than the general healthy population (10). Bone health can be improved by determining the factors that influence people with DM (11). Osteoporosis is a serious health issue that is characterized by a reduction in BMD, microarchitecture changes, and an increased risk of fracture as a direct result of these changes. Osteoporosis affects a huge number of people in both genders and in all races. The disease is expected to increase with aging. It is a disease that does not show any symptoms until fractures occur, at which point it can lead to serious secondary health issues and even death (12). The association between osteoporosis and diabetes mellitus has most consistently been evidenced in DMII patients (13). Diabetes mellitus diagnosed at an earlier age, longer duration and higher insulin doses, and prolonged periods of poor glycemic control are among the causes of greater bone mineral density loss (14). The main objectives of this study were to compare between BMD using DEXA diagnosis for normal subjects (depending on spine and hip bone mass density) and BMD diagnosis by DEXA, for other parts of the body of same individuals. To compare between the bone mineralization of both sides of the body and also between different parts of same subjects (i.e., upper and lower extremities) To compare the BMDs of males and females. To compare BMDs of healthy subjects (normal DEXA readings) with those of patients with DMII.

Materials and Methods:

This study was conducted in the Outpatient Clinic of Rheumatology, Baghdad Teaching Hospital, Medical City, Baghdad, from November 2021 to April 2022 as part of the assessment of the effects of diabetes mellitus on bone mineral density on the human body. Bone mineral density of controls and patients was measured using a DEXA scan (Company: Diagnostic Medical System - France, Version: V3.0.8.313/01/2014, License: Total Body Lateral Spine FVA pediatric DICOM Push/print DICOM Worklist Orthopedics, and Laser: power output = 1.00 mW and wavelength = 670 nm) over the entire bodies of the samples. The study involved 90 subjects randomly selected (apparently healthy) as a control, and 165 patients who visited the Clinic of Rheumatology with the chief complaint of bone pain. The age of all subjects in this study was between 20-60 years. These participants were divided into groups according to complaints of DM or otherwise, as shown in Table 1. All participants were sub-divided according to gender, as shown in Table 2.

Table 1: Distribution of study participants

Total no of participants	Healthy subjects (control)	Non-diabetic patients with bone pain	Diabetic patients with bone pain
255	90	80	85

Table 2: Gender distribution of participants

	Total number	Male	Female
Control group	90	45	45
Non-diabetic patients with bone pain	80	40	40
Diabetic patients with bone pain	85	45	40

Collection of demographic characteristics of participants. All samples (255 people) answered the questionnaire, which included smoking (cigarettes or electronics, amount of smoking), blood pressure, diabetes (type of diabetes, type of treatment, and duration of disease (years)), work (routine or hard work), dominancy side (right side or left side is dominantly used), as well as asking women about the time of menopause (pre-menopause or post-menopause). Patients who are smokers and hypertensive were excluded from the study. For all of participants, a list of questions had to be answered, with HbA1C completed by the patient group and bone mineral density measured for whole body via the DEXA instrument. Diabetes diagnosis**:** Diabetes mellitus (DM) in all samples was evaluated through blood collection and the HbA1C test performed in the biochemical analysis laboratories in the same hospital. The cumulative percentage of sugar was adopted, and the type II DM was determined.

Measurements: The whole body of all groups was examined via the DEXA device to measure the bone mineral density, the focus of this exam being on the left and right arms, and the right and left legs of women and men, separately. These measurements involved the control and the two groups of patients.

Statistical analysis

Statistical analyses were performed using Statistical Package for Social Sciences (SPSS for Windows (IBM inc.) version 22). The differences between control (normal: no osteoporosis and no diabetes), osteoporosis and type II DM with osteoporosis were analyzed using paired and unpaired t-tests according on the number of samples. Mean and standard error mean were reported and the p-value of significance was equal to or less than 0.05.

Results

Demographic characteristics of participants

The mean±SD height was 170.85 ± 1.08cm for males and 164.98 ± 0.89cm for females, as well as having mean±SD weight of 83.8 ± 3.56kg for males and 87.64 ± 2.45kg for females (Table 3).

Table 3: Demographic characteristics of the two groups (males and females) considered in this study

Variable	Males (mean±SD)	Female
Age (20 -60 years)	50.9 ± 1.88	46.2 ± 1.24
Height (cm)	170.85 ± 1.08	164.98 ± 0.89
Weight (kg)	83.8 ± 3.56	87.64 ± 2.45

SD: Standard deviation.

Bone mineral density of the spine for both genders

Table 4 demonstrates that there are no significant differences in the mean values of BMD of spine in the osteoporosis case and DM II with osteoporosis case when compared with the mean values of BMD of the control case for the female, which also applies in the case of the males.

Table 4: The mean±SD values of BMD of spine in the osteoporosis case and *DM II* with osteoporosis case

Females			Males		
Control	Osteoporosis	DMII with Osteoporosis	Control	Osteoporosis	DMII with Osteoporosis
1.08 ± 0.224	1.031 ± 0.019	0.961 0.0551 ±	1.188 ± 0.025	1.161 ± 0.019	1.145 0.0371±

Table 5: Summery of the questionnaire completed by the males and females considered in this study

Variable	Male		Female	
Normal	45		45	
Osteoporosis	40		40	
Diabetes Mellitus II with bone pain	45		40	
Type of treatment (medication) (for diabetic patients)	Insulin = 45		Insulin = 40	
The duration of diabetes mellitus (years)	Range (2- 27) years		Range (3- 25) years	
Dominancy of arm and leg (type of work; routine and hard work)	Left side = 52	Right side = 78	Left side = 49	Right side = 76

Although the DEXA scan was conducted for the whole body, including a healthy spine and hip, the reduction in bone mineral density (BMD) for different limbs in the body was recorded in this study. These findings included the effects of *DMII* with osteoporosis (85 persons) on bone mineral density, in addition to presenting the results of osteoporosis (80 persons without diabetes) and comparing them with normal bone mineral density for the 90 controls (healthy individuals) for these extremities.

Bone mineral density of the upper limbs of both genders

The *mean* value of BMD of the upper limbs (left and right arms) of the females and males involved in the current study is shown in Table (6).

Table 6 shows that there is a reduction in the mean values of BMD in the upper extremities in the females of all groups (normal, osteoporosis, and DM II with osteoporosis) when compared with the BMD of the same groups and the same side of the males. The left arm of the females revealed a reduction in the mean values of BMD of the normal, osteoporosis, DM II with osteoporosis in comparison with the mean values of BMD for controls, osteoporosis, DM II with osteoporosis of the left arm of males by 16%, 19%, and 14%, respectively. Highly significant differences ($P < 0.001$) were reported in the BMD between the mean values of the normal, osteoporosis, and DM II with osteoporosis in females in comparison with the mean values of the normal, osteoporosis, and DM II with osteoporosis in males, respectively; (Figure 1).

Table 6: Bone mineral density of the left and right arms of females and males participated in the current study

Variable	Normal	Osteoporosis	DMII + Osteoporosis
Left Arm Female	0.765 ± 0.008	0.543 ± 0.012	0.458±0.015
Left Arm Male	0.912 ± 0.032	0.673 ± 0.017	0.494±0.013
Right Arm Female	0.743 ± 0.008	0.549 ± 0.01	0.472±0.011
Right Arm Male	0.847 ± 0.024	0.653 ± 0.01	0.5±0.05

Also, for the right arm of the females, the reductions in the mean values of BMD of the normal, osteoporosis, and DM II with osteoporosis in comparison with the mean values of BMD for the normal, osteoporosis, and DM II with osteoporosis of the left arm of the males were 12%, 15%, and 10%, respectively. Highly statistically significant ($P<0.001$) differences were found in the BMD of the normal, osteoporosis, and DM II with osteoporosis for the right arm of females in comparison with the mean values of the normal, osteoporosis, and DM II with osteoporosis of the right arm of males, respectively, (Figure 1).

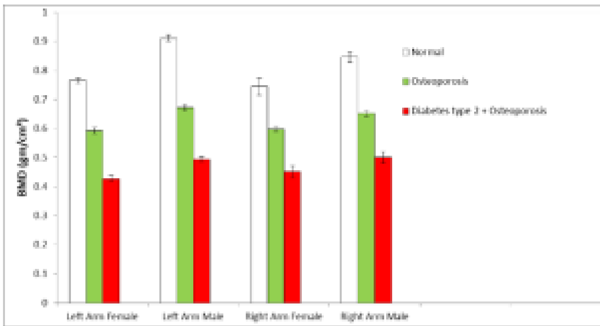

Figure 1: Comparison of the mean values of BMD for the normal BMD, osteoporosis, and DMII with osteoporosis for the left and right arms between females and males participated in the current study.

The mean value of BMD for the left arms of the females was greater than the BMD of the right arm in the healthy case by 2.9%, but it was approximately equal in the osteoporosis case and less in DM II with the osteoporosis case by 6%. The BMD for the left arms of the males was greater than the BMD for the right arm in the healthy case by 7%, and DMII with the osteoporosis case by 3%, but was approximately equal in the osteoporosis case.

Bone mineral density of the lower limbs of both genders.

The mean values of BMD for the lower limbs (left and right legs) of the females and males involved in the current study are summarized in Table 7.

Table 7 demonstrates that there is a reduction in the mean values of BMD in each group (normal, osteoporosis, and DM II with osteoporosis) in females when compared with the BMD of the same group and the same side of the males. The left legs of the females revealed reductions in the mean values of BMD for the normal, osteoporosis, and DM II with osteoporosis in comparison with the mean values of BMD for the normal, osteoporosis, and DM II with osteoporosis of the left legs of the males were 11%, 17%, and 8%, respectively. Highly significant differences (*P*<0.001) were found in the BMDs for the mean values of the normal, osteoporosis, and DM II with osteoporosis of the left legs of females in comparison with the mean values of the normal, osteoporosis, and DM II with osteoporosis for the left legs of males, respectively; (Figure 2).

Table 7: Mean values of bone mineral density of the left and right legs of females and males participated in the current study

Variable	Normal	Osteoporosis	DMII + Osteoporosis
Left Leg Female	0.865 ± 0.017	0.712 ± 0.02	0.561±0.02
Left Leg Male	0.974 ± 0.029	0.862 ± 0.01	0.617±0.03
Right Leg Female	0.972 ± 0.017	0.735 ± 0.03	0.56±0.015
Right Leg Male	1.13 ± 0.029	0.858 ± 0.01	0.591±0.02

Also, for the right legs of the females, the reductions in the mean values of BMD for the normal, osteoporosis, and DM II with osteoporosis in comparison with the mean values of BMD for the normal, osteoporosis, and DM II with osteoporosis of the right legs of the males were 13%, 14%, and 11%, respectively. Highly statistically significant ($P < 0.001$) differences were found in the BMD of the normal, osteoporosis, and DM II with osteoporosis of the right legs of females in comparison with the mean values of the normal, osteoporosis, and DM II with osteoporosis of the right legs of males, respectively, (Figure 2).

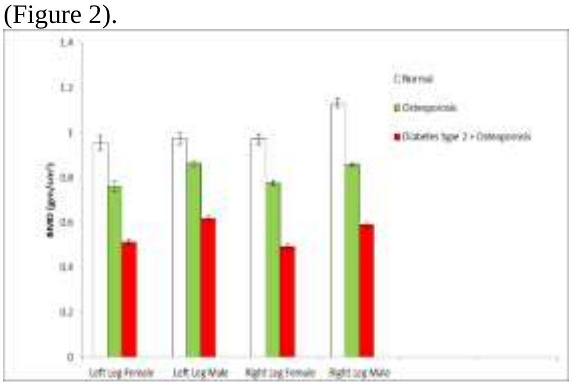

Figure 2: Comparison of the mean values of BMD for the normal, osteoporosis, and DM II with osteoporosis for the left and right legs between females and males participated in current study.

The mean values of BMD for the left legs of the females were less than the BMD for the right legs in the healthy case and osteoporosis case by 12.4% and 3.2%, respectively, but it was greater in the DM II with osteoporosis case by 6.1%. The BMD of the left legs of males was less than the BMD of the right legs in the healthy case by 16%, and approximately equal in the osteoporosis case, but it was greater in the DMII with osteoporosis case by 3%.

Discussion

Although the spine and hip bone BMD measurement is routinely used as a guide for the general assessment of BMD for the patient (13), this manner of assessment is still relatively accurate. The results of this study revealed that a large difference in BMD between the different parts of the body sometimes indicated osteoporosis, although the BMD of the spine and hip bone suggested a normal mass. This result could potentially provide the specialist, especially orthopedic surgeons, with precise information about the mineralization of the remaining parts of the body in order to treat the pathology in an appropriate way.

In the clinical diagnosis of osteoporosis, bone mineral density (BMD) measurements via DEXA scan are regarded as the gold standard. The results of the current study indicated highly significant differences between females and males in each group (normal, osteoporosis, and DM II with osteoporosis) and on the same sides for the upper limbs (left arm and right arm) (Figure 1) and lower limbs (left leg and right leg) (Figure 2). This might be due to the number of children (more than one pregnancy) and breast-feeding children with the effect of menopause. One of the studies reported that prolonged breastfeeding had a significant association with reduction in bone mineral density (BMD) in the lower spine which leads to a higher prevalence of osteoporosis (16). BMD was affected by both the number of births and the age of the mother at the time of childbirth (17). According to the findings of *Gur et al*. (2003), BMD dropped after the menopause (18, 19). These results could be due to the relationship between estrogen and BMD.

Physical activity is absolutely necessary for healthy bone growth. It is important to note that engaging in regular physical activity can result in an increase in BMD. People of any age who have active lifestyle significantly higher BMDs than people of the same age who are disabled, for instance, regardless of their age. Bone mineral density in adults can be maintained and even increased by using healthy and prepared stimuli, which can be provided by exercise (20). This agrees with this study regarding the lower limbs, where the right leg was dominant and has a larger BMD than the left leg. Although the use of the right arm is dominant, the bone mineral density was lower in comparison with the left arm. The reason behind this finding could be attributed to incorrect and irregular use, and harmful work, and incorrect exercise. These could potentially lead to a decrease in BMD of the right arm.

Moyer-Mileur et al. (2008) noted that DM II occurs at an early age, and is strongly associated with low BMD which is based on the duration (years) of the this disease, and this occurs as a result of parameters such as the way the body responds to insulin, which in turn affects the metabolism and thus affects the bone health (21). Insulin is an essential component in the modeling process that leads to peak bone mineral density. Any change in this hormone is associated with bone modeling processes that can lead to osteoporosis and osteopenia. Numerous hypotheses have been proposed as to the causes of osteopenia and osteoporosis in patients with DM II (22, 23). These studies agree with our results about the bone mineral densities of upper and lower limbs for females and males when comparing osteoporosis with DM II and osteoporosis, or between osteoporosis with DMII and the normal case, for the extremities (Figures 1 and 2).

To the best of our knowledge, although the majority of doctors depend on the results of DEXA scans of the spine for diagnosis of osteoporosis in the patient (i.e., if there is no osteoporosis, the person is normal and does not suffer from health problems associated with the bones), there is still a possibility of osteoporosis in other parts of the body, as this study revealed. Therefore, there is a significant need to carry out DEXA scans over the whole body and for each part where the patient suffers from bone pain to gain an appropriate view about the mineralization of each part of the body.

Conclusion

DEXA scans for whole body and for each part of the body separately show promising results as alternative parameters to the DEXA scan for the spine or hip only. Our results indicated that the bone mineral density of women was less than that in men in all cases (normal, osteoporosis, and DMII with osteoporosis). Also, the BMD of the right side was lower than that of the left side, although the right side was dominant in the upper limbs of both genders. In addition, the BMD of the right lower limbs was greater than for the left side, although the right side was dominant for both females and males (normal, osteoporosis, and DM II with osteoporosis). Other results obtained from this research revealed that DM II can be considered to be one of the major causes of osteoporosis in the general population.

Limitations:

The limitations of this study are its small number of subjects in each case (normal, osteoporosis, and DM I with osteoporosis), the analysis of this study suggests encouraging results. Therefore, there is a strong need to carry out complementary studies that use a larger number of patients to allow for a fuller statistical analysis and thus more accurate results to support the current study and to determine if this approach represents a reliable source of medical examination.

Also, it is essential to measure BMD among DM type II patients, and also important to compare BMD among controlled DM and uncontrolled DM patients.

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Authors' declaration:

We hereby confirm that all the Figures and Tables in the manuscript are ours. Besides, the Figures and images, which are not ours, have been given permission for re-publication attached with the manuscript.-Authors sign on ethical consideration's approval-Ethical Clearance: The project was approved by the local ethical committee in College of Medicine, University of Baghdad and with a cooperation was made with the outpatient clinic of the Medical City Teaching Hospital, according to the letter issued by the Deanship of the College of Medicine, University of Baghdad No. (1618) at (24/11/2021).

Conflict of Interest: None

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Author's contributions:
Study conception & design: (Zainab Sami Abdel Aziz). Literature search: (Zainab Sami Abdel Aziz). Data acquisition: (Zainab Sami Abdel Aziz). Data analysis & interpretation: (Zainab Sami Abdel Aziz, Maan H. Al-khalisy and Maan H. Al-khalisy). Manuscript preparation: (Zainab Sami Abdel Aziz, Maan H. Al-khalisy and Maan H. Al-khalisy). Manuscript editing & review: (Maan H. Al-khalisy).

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تقييم تأثير داء السكري 2 على كثافة المعادن العظمية للأطراف العلوية والسفلية عن طريق قياس امتصاص الأشعة السينية ثنائي الطاقة

زينب سامي عبدالعزيز / كلية الطب / جامعة بغداد
أ.م.د.نعمان سلمان داود / كلية الطب / جامعة بغداد
أ.د. معن حمد حسين الخالصي / كلية الطب / جامعة بغداد

الخلاصة:
الخلفية: تم تقييم كثافة المعادن في العظام () باستخدام مقياس امتصاص الأشعة السينية ثنائي الطاقة .(DEXA) يتم قياس كثافة المعادن بالعظام وفقا لنتائج فحص DEXA للعمود الفقري والحوض. على الرغم من أنه من المعروف أن مرض السكري () يؤثر على كثافة المعادن بالعظام ، إلا أن المعلومات المتعلقة بهذه العلاقة ليست واضحة بشكل خاص حاليا.
الهدف: كان الهدف من الدراسة الحالية هو تقييم آثار داء السكري من النوع الثاني على كثافة المعادن في العظام في الأطراف العلوية والسفلية وكذلك الفروق بين الجنسين.
طريقة العمل: تضمنت هذه الدراسة 165 مريضا يشكون من آلام في العظام (85 ذكرا و 80 أنثى) ، نصفهم يعانون من مرض السكري ، والذي يشمل كلا الجنسين. علاوة على ذلك ، تمت دراسة 90 متطوعا يتمتعون بصحة جيدة على ما يبدو واعتبروا أنهم يشكلون المجموعة الضابطة. تعرض جميع الأفراد (255) في هذه الدراسة لدراسة كثافة المعادن بالعظام عبر DEXA لجميع أجزاء الجسم.
النتائج: كشف اختبار DEXA عن فروق ذات دلالة إحصائية عالية بين جانبي الجسم في نفس الموضوع. بالإضافة إلى ذلك ، كانت هناك فروق ذات دلالة إحصائية في كثافة المعادن بالعظام بين الإناث والذكور ، وفروق ذات دلالة إحصائية عالية بين مجموعة التحكم والمرضى مع DMII .
الإستنتاجات : أشارت نتائجنا إلى أن كثافة المعادن في عظام النساء كانت أقل من تلك الموجودة في الرجال في جميع الحالات (طبيعية ، هشاشة العظام ، و DMII مع هشاشة العظام). كشفت النتائج الأخرى التي تم الحصول عليها من هذا البحث أن DM II يمكن اعتباره أحد الأسباب الرئيسية لهشاشة العظام في عموم السكان.
الكلمات المفتاحية: كثافة العظم ، مسح DEXA، داء السكري نوع 2 ، هشاشة العظام ، الأطراف العلوية والسفلية.