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Article

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

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Abstract
Background: Bone mineral density (BMD) has been assessed using Dual-Energy X-ray absorptiometry (DEXA). This procedure is considered to be of vital importance in assessing the general condition of individuals concerning their skeletal mineralization. BMD is measured according to the results of the DEXA examination of the vertebral column and pelvis. Although diabetes mellitus (D.M.)is known to affect BMD, the information regarding this relationship is not currently particularly clear. Objective: This study concentrates on the point that the assessment of BMD for the vertebral column is insuffi-cient to give a realistic and correct picture of the mineralization of the remaining part of the skeleton. Besides, this study elicited a generalized view of the mineralization of the different body parts between genders and between the left and right sides of the body. The effect of DM I on BMD was evaluated well in this research. Method: This study involved 165 patients complaining of bone pain (85 male and 80 female), about half of whom suffered from diabetes, involving both genders.
Further, 90 healthy volunteers had been studied and were considered to constitute the control group. All individuals (255) in this study were exposed to the study of their BMD via DEXA for all parts of the body. Results: The DEXA exam revealed highly statistically significant differences between the sides of the body in the same subject. In addition, there were significant differences in BMD between females and males and highly statistically significant differences between the control and patient groups with DM I. Finally, this study offered strong evidence that the BMD of the vertebral column and pelvis did not give an accurate picture of mineralization in the different parts of the body for a given subject.
In conclusion, the DEXA scan for the whole body and each part separately shows promising results as alternative parameters of the DEXA scan for the spine or hip only for accurate diagnosis. Our results indicate that the BMD of the left and right sides for women was less than for men in all cases (average, osteoporosis, and DMI with osteoporosis) for the same sides and between their upper and lower limbs. Patients with DMI revealed significant reductions in BMD in comparison with other subjects who were not diabetic, even if they had osteoporosis.

Keywords: DEXA scan, Osteoporosis, DMI, BMD

Introduction

Bone mineral density, or BMD, represents the most informative evaluation of bone quality that can be applied in clinical management. When it is higher or lower than the normal limits, this indicates health problems in the bones[1]. For example, a change in the BMD in the upper limbs (left and right arm) and lower limbs (left and right legs) increases the fracture risk. Bone mineral density scanning is an improved form of the X-ray technique, which can develop spatial resolution directional accuracy, can be rapidly implemented, and results in minimal exposure to radiation due to the short time re-quired for DEXA, which makes this technique more effective than previous ones. In order to perform the BMD evaluation, the attenuation properties of various materials within the body are calculated concerning the photon energy. There are many potential sites for the examination; however, the lum-bar 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. The most significant 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[2]. In addition, a DEXA scan can evaluate body com-ponents and differentiate between lean and fat mass based on the different attenuation properties of different tissue types. This enables the monitoring of the health condition of bones, which may lead to a reduction in BMD[3].

The World Health Organization (WHO) determined the appropriate threshold values in 1994 to diag-nose osteopenia and osteoporosis via DEXA scan. These thresholds represent the gold standard for the clinical diagnosis of osteoporosis, with the DEXA scan emerging as the best form of examination in bone densitometry. In particular, according to the T-score, the WHO classifies bone mineral density as usual when it is in the range1 of 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[4,5].

Diabetes mellitus (D.M.) is a chronic disease that affects the whole body and can lead to a wide vari-ety of complications, including cardiovascular disease, neuropathy, and osteoporosis disease[6]. DMI and DMII, despite having distinct underlying mechanisms, both contribute to an increased risk of fracture, which is caused by several factors and can be partially explained by loss of BMD[7]. The most common effect is the danger of hip or spine fracture, which is approximately 2.4 to seven times greater in DMI and approximately two to three times more in DMII than in the general healthy popu-lation[8]. Bone health can be improved by determining the factors influencing people with DMI[9].

Osteoporosis is a severe health issue characterized by a reduction in BMD, microarchitecture changes, and an increased risk of fracture as a direct result of these changes. Osteoporosis affects a vast num-ber of people in both sexes and all races. The disease is expected to increase with aging. It is a disease that does not show any symptoms until fractures occur, which can lead to secondary severe health is-sues and even death[10].

The association between osteoporosis and diabetes mellitus has most consistently been evidenced in DMI patients[11]. Diabetes mellitus diagnosed at an earlier age (which means longer duration, higher insulin doses, and prolonged periods of poor glycemic control) causes greater bone mineral density loss[12].

The main objectives of this study are:

-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 the same individual.

-To compare between the bone mineralization of both sides of the body and also between different parts of the same subject (i.e., upper and lower extremities).

-To compare the bmds of males and females.

-To study the comparison of the bmds of healthy subjects (normal dexa readings) to those of patients with dmi.

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 in the human body. Bone mineral density 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 Work list 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. All subjects in this study were between 20-60 years old. These participants were divided into groups according to com-plaints of D.M. or otherwise, as shown in Table 1. All participants were divided according to gender, as shown in Table 2.

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

Table 1. Division of participants into three groups.

	Total number	Male	Female
Control group	90	45	45
The patient group without D.M.	80	40	40
The patient group with D.M.	85	45	40

Table 2. Subdivision of the patients involved in this study according to gender.

DM= Diabetes mellitus disease

Characteristics of the samples

All samples (255 people) answered the questionnaire, which included smoking (cigarettes or elec-tronics, amount of smoking), blood pressure, diabetes (type of diabetes, type of treatment, and dura-tion of disease (years)), work (routine or hard work), dominancy side (right side or left side is domi-nantly used), as well as asking women about the time of menopause (pre-menopause or post-menopause). Subjects who were smokers and hypertensive were excluded from the study.

Subjects

Two hundred fifty-five persons represent the number of samples (male and female) involved in the current study. The control sample was 45 persons for each gender (male and female), whereas the number of patients with or without D.M. (bone pain) was 85 male and 80 female. The ranged age was between 20 to 60 years old)with means of 50.9±1.88 and46.2±1.24 years old for males and females, respectively. The mean heights were 170.85±1.08 cm for males and 164.98±0.89 cm for females, as well as having mean weights of83.8±3.56 kg for males and87.64±2.45 for females; see Table 3. A list of questions had to be answered for all of these samples, with HbA1C completed by the patient group and bone mineral density measured for the whole body via the DEXA instrument.

	Male	Female
Age (20 -60 years old)	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

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

Diabetes diagnosis

Diabetes mellitus (D.M.) 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 DMI was determined.

Measurements

The whole body of all groups was examined via the DEXA device to measure the bone mineral densi-ty. This exam focuses on the left and right arms and the right and left legs of women and men sepa-rately. These measurements involved the control and the two groups of patients.

Statistical analysis

Statistical analyses were performed using SPSS for Windows (IBMinc.) version 22. The differences between control (typical: no osteoporosis and no diabetes), osteoporosis and DMI with osteoporosis were analyzed using paired and unpaired t-tests according to the number of samples. Mean and stand-ard error mean were reported, and the p-value of significance was equal to or less than 0.05.

Results

The summary of answers to the questionnaire for both genders involved in this study is reported in Table 4.

	Male	Female
Normal	45	45
Osteoporosis	40	40
Diabetes Mellitus 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
Dominance of arm and leg (type of work; routine and hard work)	Left side = 52 Right side = 78	Left side = 49 Right side = 76

Table 4. Summary of the questionnaire completed by the males and females considered in this study.

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

Female			Male		
Control	Osteoporosis	DMI with Osteoporosis	Control	Osteoporosis	DMI with Osteoporosis
1.08±0.224	1.031±0.019	0.965±0.0581	1.188±0.025	1.161±0.019	1.155±0.0321

Table 5. The mean value of the bone mineral density of the spine for the males and females considered in this study.

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 a reduction in the mean values of BMD in the upper extremities in the females of all groups (regular, osteoporosis and DMI with osteoporosis) when compared with the BMD of the same groups and the same side of the male. The left arm of the females revealed a reduction in the mean values of BMD of the ordinary, osteoporosis, DMI with osteoporosis in comparison with the mean values of BMD for the typical osteoporosis, DMI with osteoporosis of the left arm of males by 16%, 19%, and 14%, respectively. High significant differences ($P < 0.001$) were elicited in the BMD be-tween the mean values of the ordinary, osteoporosis, and DMI in females compared to those of the ordinary, osteoporosis and DMI with osteoporosis in males, respectively; see Figure 1.

Organ	Normal	Osteoporosis	DM I + Osteoporosis
Left Arm Female	0.765±0.008	0.543±0.012	0.507±0.01
Left Arm Male	0.912±0.032	0.673±0.017	0.592±0.01
Right Arm Female	0.743±0.008	0.549±0.01	0.537±0.013
Right Arm Male	0.847±0.024	0.653±0.01	0.599±0.01

Table 6. The mean value of the bone mineral density of the left and right arms of females and males.

Also, for the right arm of the females, the reductions in the mean values of BMD of the normal, oste-oporosis, and DMI with osteoporosis in comparison with the mean values of BMD for the normal, os-teoporosis, and DMI with osteoporosis of the left arm of the males were 12%, 15%, and 10%, respec-tively. Highly statistically significant ($P < 0.001$) differences were found in the BMD of the normal, osteoporosis, and DMI with osteoporosis for the right arm of females in comparison with the mean values of the normal, osteoporosis, and DMI with osteoporosis of the right arm of males, respectively, as presented in Figure 1.

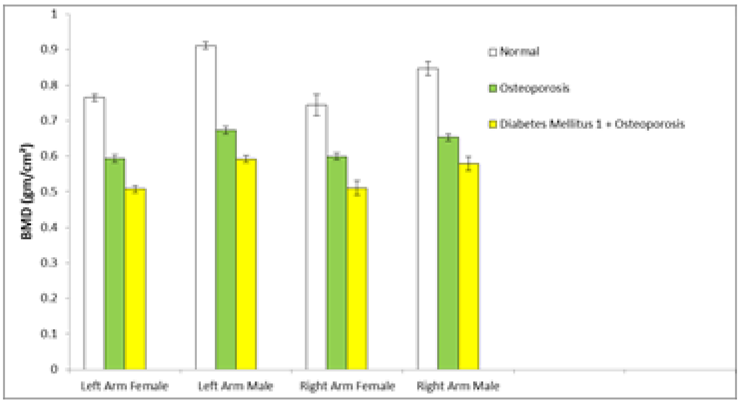

Figure 1. Comparison of the mean values of BMD for the normal BMD, osteoporosis, and DMI with osteoporosis for the left and right arms between females and males.

The mean value of BMD for the left arms of the females was more significant 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 the DM I with osteoporosis case by 6%. The BMD for the left arms of the males was more sig-nificant than the BMD for the right arm in the healthy case by 7%, and DM1 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 value of BMD for the lower limbs (left and right legs) of the females and males involved in the current study is summarized in Table 7.

Organ	Normal	Osteoporosis	DM1 + Osteoporosis
Left Leg Female	0.865±0.017	0.712±0.02	0.687±0.017
Left Leg Male	0.974±0.029	0.862±0.01	0.752±0.01
Right Leg Female	0.972±0.017	0.735±0.03	0.645±0.025
Right Leg Male	1.13±0.029	0.858±0.01	0.729±0.023

Table 7. The mean value of the bone mineral density of the left and right legs of females and males.

Table 7 demonstrates a reduction in the mean values of BMD in each group (normal, osteoporosis, and DMI with osteoporosis) in females 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 DMI with osteoporosis in comparison with the mean values of BMD for the normal, osteoporosis, and DMI 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 DMI with osteoporosis of the left legs of females in comparison with the mean values of the normal, osteoporosis, and DMI with osteoporosis for the left legs of males, re-spectively; see Figure 2.

Also, for the right legs of the females, the reductions in the mean values of BMD for normal osteo-porosis and DMI with osteoporosis in comparison with the mean values of BMD for the normal oste-oporosis and DMI with osteoporosis of the right legs of the males were 13%, 14%, and 11%, respec-tively. Highly statistically significant ($P < 0.001$) differences were found in the BMD of the normal, osteo-porosis, and DMI with osteoporosis of the right legs of females in comparison with the mean values of the normal, osteoporosis, and DMI with osteoporosis of the right legs of males, respectively, as presented in Figure 2.

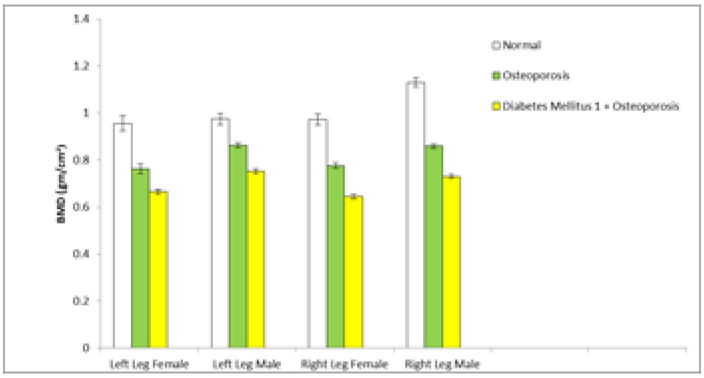

Figure 2. Comparison of the mean values of BMD for the normal, osteoporosis, and DMI with osteoporosis for the left and right legs between females and males.

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 more significant in the DM I with osteoporosis case by 6.1%. The BMD of the left legs of males was less than that of the right legs in the healthy case by 16% and approximately equal in the osteoporosis case, but it was more significant in the DM1 with osteoporosis case by 3%.
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 more significant in the DM I with osteoporosis case by 6.1%. The BMD of the left legs of males was less than that of the right legs in the healthy case by 16% and approximately equal in the osteoporosis case, but it was more significant in the DM1 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 assessment is still relatively accurate. The results of this study revealed that a significant difference in BMD between the different parts of the body sometimes indicated osteoporosis. However, the BMD of the spine and hip bone suggested an average mass. This result could provide specialists, especially orthopedic surgeons, with precise information about the mineralization of the remaining parts of the body to treat the pathology appropriately.
In the clinical diagnosis of osteoporosis, bone mineral density (BMD) measurements via DEXA scan are the gold standard. The results of the current study indicated highly significant differences between females and males in each group (average, osteoporosis, and DMI 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 breastfeeding children with the effect of menopause. One of the studies reported that prolonged breastfeeding had a significant association with a reduction in bone mineral density (BMD) in the lower spine, which leads to a higher prevalence of osteoporosis. BMD was affected by both the number of births and the mother's age at the time of childbirth[14], and according to the findings of [15], BMD dropped after menopause[15]. These results could be due to the relationship between estrogen and BMD.
Physical activity is necessary for healthy bone growth. It is important to note that engaging in regular physical activity can increase BMD. People of any age who have active lifestyles have 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[16]. This agrees with this study regarding the lower limbs, where the right leg was dominant and had a larger BMD than the left leg. Although using the right arm is dominant, the bone mineral density was lower than the left arm. This finding could be attributed to

incorrect and irregular use, harmful work, and incorrect exercise. These could lead to a decrease in BMD of the right arm.

Seventeen noted that DMI occurs at an early age and is strongly associated with low BMD, which is based on the duration (years) of 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[17]. Insulin is essential 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 regarding the causes of osteopenia and osteoporosis in patients with DMI[18]. These studies agree with our results about the bone mineral densities of upper limbs and lower limbs for females and males when comparing osteoporosis with DMI and osteoporosis or between osteoporosis with DMI and the typical 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 of the mineralization of each part of the body.

Conclusion

DEXA scans for the whole body and each part of the body show promising results as alternative parameters to the DEXA scan for the spine or hip only. Our results indicated that in all cases, women's bone mineral density was less than men's (normal, osteoporosis, and DMI 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 more significant than the left side, although the right side was dominant for both females and males (normal, osteoporosis, and DMI with osteoporosis). Other results from this research revealed that DM I can be considered one of the significant causes of osteoporosis in the general population.

Recommendation

Although 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 solid need to carry out complementary studies that use a more significant number of patients to allow for a fuller statistical analysis. 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 D.M. type II patients and compare BMD among controlled D.M. and uncontrolled D.M. patients.

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