# Dual-energy x-ray absorptiometry scan (DXA) findings in diabetic and non-diabetic female: A retrospective cohort study

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## ABSTRACT

**Introduction: Osteoporosis is a silent disease which has an effect on bone structure. Studies on the association between bone mineral density (BMD) and type 2 diabetes mellitus (T2DM) revealed conflicting results. We conducted a study to assess the prevalence of osteoporosis in females with T2DM and compare dual energy x-ray absorptiometry (DXA) scan results between diabetic and non-diabetic females in the United Arab Emirates (UAE).**

**Materials and Methods: We retrospectively analysed hospital records and DXA scan measurements of 635 patients at tertiary hospital in Ajman, UAE. Patients with T2DM were compared to non-diabetic control group. Data were analysed using SPSS version 20. Student's t test was used for continuous variables, while chi-square test for categorical variables. Relative risk (RR) and it's 95% Confidence Interval (95%CI) were calculated for prevalence of osteoporosis among the two group.**

**Results: In all 141 patients in the diabetic group and 428 patients in the control group, while 66 patients were excluded based on exclusion criteria. Prevalence of osteoporosis was significantly higher in diabetic group (RR: 1.2, 95%CI: 1.1, 1.2). BMD and T-score values were similar in diabetic and control groups. Z-score values of lumbar spine, L1 and L3 were significantly higher in diabetic group. Obese patients have significantly higher BMD than non-obese in both studied groups. Younger diabetic patient had significantly higher value of BMD, T-score and Z-score in left femur total hip.**

**Conclusion: Although BMD and T-score values were similar between the two groups, women with T2DM had significant higher prevalence of osteoporosis.**

**KEY WORDS:**
*Osteoporosis, Type 2 diabetes mellitus, Bone mineral density, Emarati women*

## INTRODUCTION

Osteoporosis is considered the most common metabolic bone disorder worldwide.[1] The inspection of osteoporosis as an international problem is anchored in the recognition of its spread across developed and developing countries,[2] and has been listed by World Health Organization (WHO) as a major non-communicable diseases.[3] According to the International Osteoporosis Foundation (IOF) audit in the Middle East and African region, 24% of people in the United Arab Emirates (UAE) have osteopenia while 2.5% suffer from osteoporosis.[4] Measurement of bone mineral density (BMD) through dual energy x-ray absorptiometry (DXA) scan is the most broadly validated technique for bone mass assessment.[5,6] The diagnosis of osteoporosis is confirmed based on the T-score of BMD.[6] The International Society for Clinical Densitometry (ISCD) prefers the use of Z-score over T-score for diagnosis of osteoporosis in premenopausal women, men less than 50 years of age, and children.

The WHO criteria for assessment of BMD is based on classifying T-score into the three categories: ''normal (T-score ≥ -1.0), osteopenia (T-score between -1.0 and -2.5) and osteoporosis (T-score ≤ -2.5)''.[2] Fracture Risk Assessment tool (FRAX®) integrate clinical risk factors and BMD to provide 10-year probability of hip fracture and major osteoporotic fracture.[8]

Diabetes is among the most widespread chronic diseases in many countries, due to changes in lifestyles, associated with increase obesity and decrease physical activity.[9] Based on international diabetes federation (IDF) 2017 update, there are 425 million people suffering from diabetes globally, and 1 in 11 adults in Middle East and North African region has diabetes. UAE ranked the 8th in Middle East and North African region in prevalence of diabetes, with more than one million cases of diabetes in 2017.[10]

The relationship between BMD and type 2 diabetes mellitus (T2DM) is characterised by vast controversial, with variation toward higher,[11-13] normal[14-16] and lower values of BMD in patient with T2DM.[17-19] A better understanding of the effect of diabetes mellitus on bone architecture will help to improve prevention of fracture,[20] and international guideline in favour of patients. The WHO scientific group on the assessment of osteoporosis at primary health care level recommend further research work on secondary causes of osteoporosis.[5] No study has looked at the association between osteoporosis and T2DM among Emarati (UAE) females.

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In this study we intend to assess the association between osteoporosis and T2DM in females, with an emphasis on the identification of major characteristic of BMD, T-score and Z-score in female diabetic patients.

## MATERIALS AND METHODS

*Study design, data source and exclusion criteria*

This is a retrospective cohort study on female patients referred to DXA scan in X-ray department at tertiary hospital in Ajman, UAE between 24 July 2010 and 25 December 2012. All electronic records were reviewed, using the hospital database.

Patients were assigned index date; the time when the electronic record was opened in the hospital database. Demographic data and clinical history was collected from the index date until the end of study. Data reflect patients with confirmed diagnosis of diabetes during study period. The result of first DXA scan done for each patient was the one used in the analysis. DXA scan instrument was installed in the hospital in July 2010.

Exclusion criteria were: (1) individuals with type 1 diabetes mellitus (T1DM), (2) males (3) patients age <25 years and those who (4) lack electronic record in the hospital database. T1DM was identified as there is confirmed diagnosis in patient's record of diabetes mellitus, with medications restricted to insulin only.

*Study participants*

Patients with T2DM were compared with non-diabetic control group. We defined individuals as having T2DM according to the following criteria: (1) confirmation of the diagnosis of T2DM in patient record or (2) use of oral antidiabetic medications, or (3) a fasting plasma glucose ≥126mg/dl (7.0mmol/l) or a 2-h post-load glucose ≥200mg/dl (11.1mmol/l) during an oral glucose tolerance test. Females were considered postmenopausal if: (1) age ≥50 years, or (2) age ≤50 years with documentation in her file that the patient is postmenopausal. Patient were identified as suffering from osteoporosis if: (1) there was confirmed diagnosis in their record, or (2) T-score ≤ -2.5 in the lumbar spine, femoral neck or total hip,[22] or (3) receiving antiresorptive agents or bone-forming agent e.g., teriparatide.

*Demographic data and clinical history*

Hospital database contains details medical information including demographic information (gender and age), nationality, inpatient hospitalisation and visits to outpatient clinics, as well as laboratory result, requested X-rays, prescribed medications, diagnosis and contact information.

Height, weight and BMI values were taken from Eazix software of DXA scan instrument (Osteocore 3 desintometer, Medilink Inc, France), and was interpreted according to the WHO criteria: BMI less than 18.5 as underweight, between 18.5 and 25 normal, greater than 25 overweight and above 30 obese.[22]

*Dual Energy X-ray Absorptiometry scan*

DXA scan radiograph results were taken from Eazix software of DXA scan instrument. Lumbar spine (L1-L4) BMD, left femur-total hip BMD, T-score and Z-score results were collected. BMD values were expressed as absolute values in grams per square centimetre. T-score and Z-score were expressed as absolute standard deviation (SD) values and were compared in software to matched reference population supplied by the manufacture.

*Statistical analysis*

Data were analysed using SPSS version 20. Mean and SD were calculated for different continuous variables, and student's t test was used to compare mean values to test the significance level. Categorical variables are expressed as percentage, and chi-square test was used to assess the statistical significance level. Relative risk (RR) and its 95% Confidence Interval (95%CI) were obtained from cross-tabulation. The level of significance was at p≤0.05.

## RESULTS

We identified 635 patients who had DXA scan between 24 July 2010 and 25 December 2012. Sixty-six patients were excluded based on exclusion criteria, giving a final number of 569 patients; 141 in the diabetic group and 428 in the control group. Mean follow-up period of patients was 35.66±11.63 months.

General characteristics of patients is shown in (Table I). Most patients were elderly, with mean age of 63.55±9.15 years in diabetic group, and 58.88±11.71 years in control group. Obesity accounts for high percentages in both groups, and generally patients were either overweight or obese. Mean BMI value in the diabetic group was 30.27±6.73 and 29.78±5.66 in the control group. It was noticeable that more than half the numbers of patients were from the UAE, with significantly higher percentages in the diabetic group (p≤0.001). Additionally, postmenopausal females accounted for 92% from the whole sample. Prevalence of osteoporosis was significantly higher (p≤0.01) in the diabetic group compared with the control group (RR=1.2, 95%CI: 1.1, 1.2), despite similar percent of patients with T-score ≤ -2.5 in both groups. It is clear from Table II that BMD and T-score values are similar in the diabetic and control groups. Z-score values of lumbar spine, L1 and L3 were significantly higher (p≤0.05) in the diabetic group than control group. Stratifying DXA scan output by age clarify different pattern of results shown in (Table III). Diabetic patients within age range of 40–49 years had significantly higher value (p≤0.05) of BMD, T-score and Z-score of left femur total hip compared to the control group. In addition, diabetic patients in the age range of 50–59 years have significantly higher value of BMD and Z-score in L3 region of spine than another group. There were roughly similar values of BMD, T-score and Z-score in patients ≥60 years of age in both groups.

Results of stratified patients according to obesity is shown in Table IV. Comparing obese patients with non-obese within each group showed significantly higher BMD values in obese diabetic patients at the lumbar spine, L3 and left femur-total hip. Likewise, BMD value in obese control patients were significantly higher (p≤0.001) in all studied skeletal region than non-obese from same group. T-score and Z-score values were significantly higher in some skeletal site in obese diabetic patient compared to all skeletal sites in obese patients of the control group.

**Table I: General characteristics of patients in diabetic and control groups**

| Variable | Diabetes (n=141) | Control (n = 428) | Total (n = 569) |
|---|---|---|---|
| Age (years) | 63.55 ± 9.15 | 58.88 ± 11.71*** | 59.96 ± 11.45 |
| Height (cm) | 158.44 ± 5.84 | 158.33 ± 5.51 | 158.36 ± 5.59 |
| Weight (Kg) | 76.19 ± 18.34 | 75.02 ± 16.01 | 75.31 ± 16.61 |
| BMI (Kg/m2) | 30.27 ± 6.73 | 29.78 ± 5.66 | 29.90 ± 5.94 |
| Emarati % (n) | 74.1 (103) | 58.2 (244)*** | 62.2 (347) |
| Menopausal status | | | |
| Pre-menopausal % (n) | 5 (7) | 8.9 (38) | 7.9 (45) |
| Post-menopausal % (n) | 95 (134) | 91.1 (390) | 92.1 (524) |
| Fracture % (n) | 9.9 (14) | 9.3 (40) | 9.5 (54) |
| Osteoporosis % (n) | 72.3 (102) | 60.5 (259)** | 63.4 (361) |
| T-score ≤-2.5 % (n) | 35.5 (49) | 34.5 (146) | 34.8 (195) |

Values are percent or means ± SD, * P≤0.05, ** P≤0.01, *** P≤0.001, BMI: body mass index

**Table II: BMD, T-score and Z-score in diabetic and control groups**

| Variable | Diabetes (n = 141) | Control (n = 428) | Total (n = 569) |
|---|---|---|---|
| BMD (g/cm2) | | | |
| Lumbar spine (L1-L4) | 0.89 ± 0.20 | 0.90 ± 0.20 | 0.90 ± 0.20 |
| L1 | 0.89 ± 0.36 | 0.86 ± 0.23 | 0.87 ± 0.27 |
| L2 | 0.89 ± 0.26 | 0.89 ± 0.24 | 0.89 ± 0.25 |
| L3 | 0.90 ± 0.28 | 0.90 ± 0.23 | 0.90 ± 0.25 |
| L4 | 0.95 ± 0.33 | 0.96 ± 0.31 | 0.96 ± 0.32 |
| Left femur-total hip | 0.88 ± 0.18 | 0.90 ± 0.18 | 0.89 ± 0.18 |
| T-score (SD) | | | |
| Lumbar spine (L1-L4) | -0.72 ± 1.89 | -0.71 ± 1.87 | -0.72 ± 1.88 |
| L1 | -0.30 ± 2.38 | -0.21 ± 2.04 | -0.22 ± 2.12 |
| L2 | -0.69 ± 2.03 | -0.69 ± 2.00 | -0.69 ± 2.01 |
| L3 | -1.03 ± 2.05 | -1.04 ± 2.05 | -1.04 ± 2.04 |
| L4 | -1.04 ± 2.06 | -0.81 ± 2.38 | -0.86 ± 2.31 |
| Left femur-total hip | 0.30 ± 1.57 | 0.45 ± 2.41 | 0.41 ± 2.23 |
| Z-score (SD) | | | |
| Lumbar spine (L1-L4) | 0.94 ± 1.71 | 0.60 ± 1.84* | 0.69 ± 1.81 |
| L1 | 1.29 ± 1.55 | 0.95 ± 1.86* | 1.03 ± 1.79 |
| L2 | 0.91 ± 1.79 | 0.65 ± 2.05 | 0.72 ± 1.99 |
| L3 | 0.73 ± 1.89 | 0.33 ± 2.02* | 0.43 ± 1.99 |
| L4 | 0.79 ± 1.98 | 0.51 ± 2.12 | 0.58 ± 2.09 |
| Left femur-total hip | 1.66 ± 1.38 | 1.51 ± 2.07 | 1.54 ± 1.92 |

Values are means ± SD, * P≤0.05, ** P≤0.01, *** P≤0.001, BMD: bone mineral density

**Table III: BMD values in diabetic and control groups stratified by age**

| Variable | Age | LS | | L1 | | L2 | | L3 | | L4 | | LF-TH | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | (years) | Diabetes | Control | Diabetes | Control | Diabetes | Control | Diabetes | Control | Diabetes | Control | Diabetes | Control |
| | 40-49 | 1.03 | 0.99 | 0.99 | 0.94 | 1.02 | 0.99 | 1.05 | 0.99 | 1.05 | 0.99 | 1.09* | 0.97 |
| | 50-59 | 0.96 | 0.92 | 0.91 | 0.88 | 0.95 | 0.91 | 1.01** | 0.90 | 1.04 | 0.96 | 0.94 | 0.93 |
| | ≥60 | 0.84 | 0.84 | 0.87 | 0.82 | 0.84 | 0.83 | 0.84 | 0.85 | 0.89 | 0.94 | 0.84 | 0.83 |
| | 40-49 | 0.60 | 0.12 | 1.04 | 0.55 | 0.74 | 0.33 | 0.50 | -0.26 | 0.11 | -0.22 | 2.16* | 1.04 |
| | 50-59 | -0.02 | -0.61 | 0.29 | -0.06 | 0.04 | -0.50 | -3.37 | -0.97 | -0.54 | -0.77 | 0.81 | 0.92 |
| | ≥60 | -0.02 | -0.61 | 0.29 | -0.06 | 0.04 | -0.50 | -3.37 | -0.97 | -0.54 | -0.77 | 0.81 | 0.92 |
| | 40-49 | 1.00 | 0.53 | 1.47 | 0.92 | 1.13 | 0.99 | 0.94 | 0.18 | 0.56 | 0.27 | 2.43* | 1.35 |
| | 50-59 | 0.94 | 0.37 | 1.22 | 0.82 | 0.89 | 0.46 | 0.71* | 0.01 | 0.59 | 0.26 | 1.59 | 1.68 |
| | ≥60 | 0.94 | 0.87 | 1.32 | 1.12 | 0.90 | 0.72 | 0.72 | 0.67 | 0.91 | 0.87 | 1.63 | 1.43 |

**Table IV: BMD values in diabetic and control group stratified by obesity**

| Variable | Obesity status | LS | | L1 | | L2 | | L3 | | L4 | | LF-TH | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Diabetes | Control | Diabetes | Control | Diabetes | Control | Diabetes | Control | Diabetes | Control | Diabetes | Control |
| BMD | obese | [a]0.94** | [b]0.97*** | [a]0.91 | [b]0.95*** | [a]0.91 | [b]0.95*** | [a]0.96* | [b]0.98*** | [a]0.98 | [b]1.06*** | [a]0.93** | [b]0.95*** |
| | nonobese | 0.85 | 0.84 | 0.88 | 0.78 | 0.87 | 0.83 | 0.86 | 0.86 | 0.92 | 0.87 | 0.84 | 0.85 |
| T-score | obese | [a]-0.20** | [b]-0.01*** | [a]0.05 | [b]0.57*** | [a]-0.34 | [b]-0.10*** | [a]-0.34*** | [b]-0.37*** | [a] -0.61* | [b]-0.01*** | [a]0.65** | [b]0.93*** |
| | Nonobese | -1.14 | -1.34 | -0.59 | -0.91 | -0.98 | -1.21 | -1.59 | -1.63 | -1.39 | -1.50 | 0.01 | 0.02 |
| Z-score | obese | [a]1.22 | [b]1.21*** | [a]1.65** | [b]1.61*** | [a]1.12 | [b]1.12*** | [a]1.20** | [b]0.91*** | [a]0.10 | [b]1.17*** | [a] 1.84 | [b]2.01*** |
| | nonobese | 0.72 | 0.07 | 0.10 | 0.37 | 0.74 | 0.24 | 0.35 | -0.18 | 0.63 | -0.06 | 1.51 | 1.05 |

a vs nonobese diabetic, b vs nonobese control, * P≤0.05, ** P≤0.01, *** P≤0.001, BMD: bone mineral density, LS: lumbar spine, LF-TH: left femur-total hip

## DISCUSSION

This study was conducted at a tertiary hospital in Ajman, UAE where local patients have insurance coverage. This may be the reason for high percent of Emarati (UAE) patients in our sample as shown in (Table I).

In 2017 UAE ranked as the 12th fattest country in the world, with prevalence of 37.2% of the population.[23] Study by Sulaiman and colleagues assessing prevalence of obesity and related non-communicable diseases in UAE, found that 75% of subjects were either overweight or obese.[24] These results confirm our finding about obesity and overweight distribution which was high in both groups.

Schwartz commented that increased body weight related with T2DM patients provides protective effect against fracture.[20] However in a Norwegian prospective cohort study by Meyer and colleagues found that diabetes mellitus gave important risk of fracture (RR: 5.81, 95%CI 2.15, 15.71) in women and (RR: 7.67, 95%Cl 2.40, 24.53) in men.[25] Also meta-analysis accomplished 16 appropriate case-control and cohort studies demonstrated increase risk of hip fracture with type 1 and type 2 diabetic patients, and researcher linked this to diabetic complications such as retinopathy and neuropathy which could increase risks of falls.[26] On the other hand Vamamoto and colleagues concluded in their study about vertebral fracture (that increase fractures risks in T2DM patients) is independent of BMD or diabetic complications, hypothesize about bone quality as predominant in fragility risk.[13] They validated their hypothesis by their finding from another research, which showed that correlation between serum pentosidine level and presence of vertebral fracture.[27] Pentosidine is glycation end product which affects collagen architecture leading to deterioration in bone strength and quality, regardless of high BMD value.[27]

Our finding supports previous studies partially, since we noticed that higher but non-significant fracture rate in diabetic patient, which may be related to inadequate sample size to detect a difference, or the inadequate follow-up period, or the short duration of being diabetic, or the good control of diabetes.

Regarding the prevalence of osteoporosis in T2DM patients, Viegas and colleagues demonstrated high prevalence of osteoporosis in postmenopausal women.[28] Al-Maatouq and colleagues presented similar finding in Saudi postmenopausal women.[29] In contrast Bartos and colleagues showed no difference in prevalence of osteoporosis between postmenopausal diabetic patients and control group.[30]

Our results showed significantly higher ($p \leq 0.01$) percent of osteoporotic cases in the diabetic group.

When comparing BMD and T-score values between diabetic and control groups, we found that both groups had approximately similar values. This result supports finding from previous reports by Sosa et al, Hampson et al , Tuominen et al and Ay et al.[15,31-33] But came in opposite direction from studies that found higher[11-13] or lower values.[17-19]

Our finding of significant higher Z-score value in T2DM patients, support the conclusion of meta-analysis by Vestergaard when he noticed that pooled Z-score values from different studies elucidated increase spine and hip Z-score in T2DM patients.[26]

Finding related to significant higher prevalence of osteoporosis in the diabetic group, despite similar values of BMD and T-score between both study group may be justified for physician to start patients on antiresorptive agents or bone-forming agent regarding Fracture Risk Assessment tool (FRAX®) result as recommend by A Clinical Practice Guideline from the American College of Physicians,[34] and which our study defined as osteoporosis.

Upon stratifying DXA scan output by age we noticed that younger diabetic patients had significantly higher value of BMD, T-score and Z-score up to of age 60 years. This finding gives us insight that (1) diabetes mellitus may have protective effect on bones up to certain age (60 years), or (2) the deterioration effect of diabetes mellitus starts after the age of 60 years. There is evidence from studies that insulin enhances bone formation.[35] Stolk and colleagues found that an increase in glucose and insulin levels lead to an increase in BMD values.[36] Study by Barrett-Connor & Holbrook found that older woman with hyperglycemia had better BMD values than normoglycemic women.[37] In addition, a study demonstrated that for each 10μU/ml increase in fasting insulin level there is an increase of 0.33 and 0.57g/cm$^2$ of the radius and spine BMD, respectively.[38] Previous studies support the first justification.

Schwartz commented about the effect of accelerated bone loss in elderly diabetic patients as a contributor of bone strength deterioration.[20] Study by Kwon and colleagues in T2DM patients observed that after the age of 55 years there was abrupt loss of bone in the lumbar spine ($p \leq 0.05$).[39] These finding support the second justification. As far as we know, the present study is the first study assess the difference in BMD, T-score and Z-score between the age groups.

As shown earlier, when we stratified DXA scan results according to obesity status, obese patients showed higher value of BMD, T-score and Z-score. This support the findings reported by So and colleagues that obese patients had higher BMD value at lumbar spine and hip.[40] In conclusion, this research reported that most of the referred females for DXA scan were postmenopausal with high BMI values. Prevalence of osteoporosis was significantly higher among diabetic patients, despite similar values of BMD and T-score between the two groups. We noticed also that obese patients had significantly higher value of BMD, T-score and Z-score compared to non-obese patients, which suggests the protective effect of obesity on bone architecture.

We also recommend DXA scan examination as a follow up tool for diabetic patients beside regular assessment of glycaemic status and complication existence.

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