Original Article

Assessment of osteoporosis in patients with type 2 diabetes mellitus

A study from the central region of Saudi Arabia

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ABSTRACT

الأهداف: لتقييم تأثير داء السكري على كثافة المعادن في العظام وما إذا كان داء السكري عامل من عوامل خطر الإصابة بمرض هشاشة العظام.

المنهجية: أجريت هذه الدراسة على 327 سعوديًا (أعمارهم أكبر من 40 عامًا) وقد تم فحصهم للكشف عن هشاشة العظام ومرض السكري. وقد تم تحديد مستويات هشاشة العظام لديهم عن طريق تقدير كثافة المعادن بالعظام باستخدام الفحص بجهاز الأشعة DEXA. وتمت مقارنة القيم الخاصة بكثافة المعادن بالعظام لدى الأشخاص المصابين بمرض السكري مع مجموعة من الأصحاء غير المصابين بداء السكري.

النتائج: أظهرت النتائج أن عدد المصابين بهشاشة العظام من بين أفراد العينة هي 38 مريضا (11.6%)، وكان من بين افراد العينة 138 مريضا (42.2%) مصابون كذلك بمرض السكري. كما أظهرت البيانات أن عدد المرضى الذين يعانون من هشاشة العظام في مجموعة المصابون بمرض السكري كان 14 (36.8%)، أقل بكثير من المرضى غير المصابين بمرض السكري، 21 (55.2%) (P=0.0015). واتضح كذلك من النتائج عدم وجود فرق معنوي في كثافة المعادن (T Score) في عظم الفخذ في المرضى الذين يعانون من مرض السكري والذين لا يعانون من مرض السكري (P=0.4746). وجد أن مستويات كثافة المعادن بالعظام في العمود الفقري لدى الأفراد المصابون بداء السكري كانت أعلى بشكل ملحوظ عند مقارنتها بأصحاء غير مصابين بداء السكري (P=0.0031).

الخلاصة: وجد أن كثافة المعادن بالعظام القطنية لمرضى السكري أعلى بكثير من مثيلاتها في الأفراد الأصحاء غير المصابين بالسكري، في حين لم يكن هناك فروق معنوية في كثافة المعادن بعظم الفخذ بين كلتا المجموعتين. علاوة على ذلك، كان معدل انتشار مرض هشاشة العظام أقل لدى مرضى السكري مقارنة بالأفراد الأصحاء غير المصابين به.

Objectives: To understand the impact of diabetes on bone mineral density and whether it increases the likelihood of osteoporosis.

Methods: This study was performed on 327 Saudis (aged >40 years) who were screened for osteoporosis and diabetes mellitus (DM). The levels of osteoporosis were determined by an estimation of Bone mineral density (BMD) using a DEXA scan examination. The data on BMD from diabetic subjects were compared with healthy nondiabetic controls.

Results: Out of 327 enrolled subjects, 38 (11.6%) were found to be osteoporotic, whereas 138 (42.2%) had DM. The data showed that the number of patients with osteoporosis in the DM group was 14 (36.8%), significantly lower than in nondiabetic patients, 21 (55.2%) (p=0.0015). Notably, the data showed no significant difference in the mean BMD of the femur in patients with DM (0.926 g/cm^2) and non-diabetes (0.936 g/cm^2) (p=0.280; T-score p=0.4746). The mean BMD levels in the spine of the DM study group (1.049 g/cm^2) were significantly higher when compared with nondiabetic healthy controls (0.990 g/cm^2) (p=0.0031).

Conclusion: Patients with diabetes had higher lumbar BMD than nondiabetics, although femoral BMD was similar. Patients with diabetes have a lower osteoporosis risk than nondiabetics.

Keywords: bone mineral density, osteoporosis, type 2 Diabetes

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Type 2 diabetes mellitus (T2DM) is one of the most common metabolic disorders and has now become one of the world's major health problems, affecting nearly all organs, and its prevalence is continuously accelerating in all over the globe, particularly in developing countries.[1] Recent data showed that 8.8% of adults worldwide got DM in 2015, and this number is expected to rise to 10.4% by 2040.[2] From 1980 to 2008, the prevalence of diabetes ranged from 9% to 22% in the Kingdom of Saudi Arabia (KSA).[3] Importantly, the International Diabetes Federation (IDF) ranked Saudi Arabia among the top ten countries reported to have the highest number of diabetic cases globally.[1] Interestingly, it is documented that obesity is a risk factor in Saudi diabetic patients, which is expected to be one of the highest in the world.[4]

Osteoporosis is a well-known common systemic bone disorder that decreases the strength of bones, which directly increases the chances of bone fractures in humans.[5] The balance between osteoclast resorption and osteoblast production determines the integrity of bone microarchitecture. Early diagnosis and treatment of osteoporosis can help reduce osteoporosis-related fractures, thus minimizing public health problems.[5] Numerous studies from several parts of the world point out that osteoporosis-related morbidity has been accelerating significantly, which has a direct or indirect impact on the quality of public health. The global occurrence of osteoporosis was higher in women as compared to men.[5] In KSA, the occurrence of osteoporosis is reported to be higher than that in Western countries.[6]

It is now well documented that diabetes mellitus (DM) causes abnormal changes in the endocrine and metabolic activities that directly or indirectly impact calcium homeostasis and bone metabolism and ultimately result in bone loss.[7,8] Type 2 diabetes mellitus is one of the risk factors for fragility fractures. The role of bone mineral density (BMD) in patients with diabetes is well reported, but the pathophysiological outcomes from different research groups are controversial.[9–11] Some studies show an increase in BMD in DM patients,whereas others show a decrease and a few studies show no change in BMD.[9-11] BMD is an important biomarker for predicting the risk of fracture onset. Bone mineral density, which is noticeably higher in T2DM compared to the general population, can, however, underestimate the increased fracture risk associated with T2DM. Although BMD obtained from dual-energy x-ray absorptiometry (DEXA) scan remains a reliable predictor of fracture risk in patients with T2DM, other data (such as trabecular bone score (TBS), skeletal geometry, vertebral fracture assessment, and body composition) that can be collected from DEXA scan help in the identification of patients who are at higher risk of having fractures. The incorporation of this additional data into risk assessment models may reduce the likelihood of underestimating the fracture risk associated with osteoporosis in T2DM.[12] The pathophysiological mechanisms of increased bone fragility in DM are complex and include poor glycemic control, low bone turnover, and advanced glycation end products accumulation, leading to alterations in biochemical functions and impaired bone strength. Oxidative stress and its associated biomolecular alterations also contribute to increased fragility fracture in diabetic patients by releasing inflammatory mediators such as adipokines, which may alter osteocyte function. Other factors that may increase the risk of fracture in diabetes are antidiabetic medications, including insulin, sulfonylureas, and thiazolidinediones, which have direct effects on bone and mineral metabolism. Diabetes complications, such as neuropathy, orthostatic hypotension, poor balance, and vision loss, are also risk factors for bone fracture. It has now been well established that the prevalence of osteoporosis is on the rise just like DM generally in aging populations, which definitely increase the chances of fracture in elderly.[13]

It is now well documented that DM and osteoporosis are 2 clinical disorders that majorly impact public health due to their effects on a large proportion of the world's population.

The effect of DM on BMD is considered a current interest. To the best of our knowledge, only a few published studies have looked into the relationship between DM and BMD in the Saudi population.[14] In this study, we explored an assessment of osteoporosis in Saudi patients with T2DM. Our novel findings provide an important insight into the effects of diabetes on BMD.

Methods. A retrospective study was carried out on 327 Saudi patients (218 females and 109 males). The subjects were selected randomly from the patients visiting our hospital for osteoporosis screening. Patients attending outpatient internal medicine and orthopedic clinics at the private hospital, Dr. Sulaiman Al-Habib in Al Qassim, Saudi Arabia, were enrolled between August

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2020 and August 2021. They were classified into 3 groups: nondiabetic, prediabetic, and diabetic. The data on BMD from diabetic subjects were compared to that of healthy nondiabetic control groups. Saudi patients aged ≥40 years screened for osteoporosis and DM were included in the study with no gender or weight restrictions. Patients with chronic diseases that can lead to secondary osteoporosis, such as Cushing's syndrome, and patients on long-term steroids were excluded. Ethics approval of this study was taken from the Institutional Review Board of Dr. Sulaiman Al Habib Medical Group, Saudi Arabia (Ethical approval # RC21.11.16). Written informed consent was obtained from all participants. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Measurement of BMD and Assessment of osteoporosis. Bone mineral density (BMD) was assessed using a DEXA scan densimeter (Encore version 18, 2019 Lunar Model) using x-ray equipment and a computer to measure bone density at the lumbar spine and proximal femur, as described previously.[10] Briefly, BMD measurements of the spine were used to establish or confirm the diagnosis of osteoporosis to predict future fracture risk using a reference range of BMD. The difference between the patient's BMD and BMD reference range yields the T-score. As defined by the World Health Organization (WHO), osteoporosis is considered when BMD is 2.5 SD or more below the average value for healthy individuals (a T-score of <–2.5 SD). A second, higher threshold describes "low bone mass" or osteopenia as a T-score that lies between –1 and –2.5 SD. "Severe" or "established" osteoporosis denotes osteoporosis that has been defined in the presence of one or more documented fragility fractures. Therefore, similar approach was applied in this study for the diagnosis of osteoporosis using T-score values as described previously.[15]

Measurement of blood sugar. Type 2 diabetes mellitus was diagnosed in the studied population using following the criteria set by the American Diabetes Association (ADA). Briefly, patients with a glycated hemoglobin (HbA1c) level of ≥6.5% (48 mmol/mol) were considered diabetic. We also used the criteria for diagnosis using plasma glucose measured in the fasting state (≥126 mg/dL [7.0 mmol/L]) or 2 hours after an oral glucose load (≥200 mg/dL [11.10 mmol/L]) as defined by the ADA. The presence of fasting plasma glucose levels between 100 mg/dL (5.6 mmol/L) and 125 mg/dL (6.9 mmol/L) and/or a HbA1c of 5.7–6.4% (39–47 mmol/mol) were used to identify patients with prediabetes.[16]

Statistical analysis. The data were analyzed by Statistical Package for the Social Sciences for Windows, version 20 (IBM Corp., Armonk, N.Y., USA). Excel Microsoft software using ANOVA, and the Chi-square test, followed by Tukey-Kramer Post Hoc Test. A p-value of <0.05 was considered statistically significant.

Results. A total of 327 patients were enrolled in this study, including 66.7% females and 33.3% males screened for osteoporosis and diabetes. The prevalence of diabetes was 42.2% (138/327), whereas the prevalence of prediabetes was 17.4% (57/327). The mean age of patients with diabetes among the whole group, men and women, is significantly higher than that of prediabetic and non-diabetic patients. Although there was no significant difference in the mean of the BMI for total patients and women among the three groups (p=0.0518), both pre-DM and DM groups showed a tendency to be obese (BMI >30 kg/m^2). The demographic characteristics and measured values of total patients, men and women, among the three groups are shown in **Table 1**.

There was no significant difference in the mean BMD and T-score of the femur for the whole group, men and women, among the three groups. The mean BMD and T-score of the spine in the DM group were higher than those in the non-DM group for the whole group, men and women. The difference was statistically significant for the whole group and men, but not for women.

The prevalence of osteoporosis among the whole group was 11.6%, whereas the prevalence of osteopenia was 40%. Patients with diabetes had a prevalence of osteoporosis of 36.8%, considerably lower than that of individuals without diabetes (55.7%; p=0.0015). They also had a higher prevalence of osteopenia (43.5%) than individuals without diabetes (p=0.0005). The prevalence of osteoporosis in diabetic patients among men and women was lower than in the non-diabetic group.

Discussion. This study from the central region of Saudi Arabia that demonstrated osteoporosis in patients with T2DM. Bone mineral diseases are one of the diabetic complications that can have a negative impact on quality of life. This study demonstrated that the mean BMD and T-values of the femur and lumbar spine were higher in patients with diabetes than in those with no diabetes. The difference was statistically significant in the lumbar spine but not in the femur. In addition,

Table 1 - The demographic characteristics and measured values of total patients, men and women, among the 3 groups.

Variables	Non-DM	Pre-DM	DM	*P*-value
Whole group, n=327 (%)	132 (40.36)	57 (17.43)	138 (42.20)	<0.001
Age (years)*	56.2 ± 12.0	59.8 ± 10.4	65.9 ± 10.1	
BMI (Kg/m^2)*	29.7 ± 6.4	31.8 ± 5.2	31.2 ± 6.2	0.0518
Femur T score*	-0.402 ± 1.166	-0.172 ± 0.989	-0.301 ± 1.322	0.4746
Spine T score*	-1.016 ± 1.522	-0.479 ± 1.168	-0.590 ± 1.390	0.0069
Femur BMD, (g/cm^2)*	0.926 ± 0.161	0.966 ± 0.144	0.936 ± 0.163	0.2797
Spine BMD, (g/cm^2)*	0.990 ± 0.155	1.061 ± 0.144	1.049 ± 0.176	0.0031
Normal BMD, n= 158 (%)	60 (37.97)	31 (19.62)	67 (42.41)	0.0009
Osteopenia, n= 131 (%)	51 (38.93)	23 (17.56)	57 (43.51)	0.0005
Osteoporosis, n= 38 (%)	21 (55.26)	3 (7.90)	14 (36.84)	0.0015
Men, n=109 (%)	37 (33.94)	23 (21.1)	49 (44.95)	
Age (years)*	52.6 ± 12.7	60.9 ± 10.5	70.1 ± 11.1	<0.001
BMI (Kg/m^2)*	27.0 ± 4.4	30.8 ± 4.5	28.9 ± 6.4	0.0363
Femur T score*	-0.708 ± 1.121	-0.313 ± 0.894	-0.451 ± 1.042	0.3175
Spine T score*	-0.875 ± 1.245	-0.143 ± 1.014	-0.045 ± 1.458	0.0118
Normal BMD, n=59(%)	18 (30.5)	15 (25.42)	26 (44.06)	
Osteopenia, n= 42(%)	13 (30.96)	8 (19.04)	21 (50)	
Osteoporosis, n= 8(%)	6 (75)	0 (0)	2 (25)	
Women, n=218 (%)	95 (43.57)	34 (15.59)	89 (40.82)	
Age (years)*	57.6 ± 11.6	59.1 ± 10.4	63.6 ± 8.7	0.0005
BMI (Kg/m^2)*	30.8 ± 6.8	32.4 ± 5.5	32.5 ± 5.8	0.1363
Femur T score*	-0.282 ± 1.167	-0.076 ± 1.051	-0.218 ± 1.452	0.7216
Spine T score*	-1.071 ± 1.260	-0.706 ± 1.224	-0.889 ± 1.262	0.3099
Normal BMD, n=99(%)	42 (42.42)	16 (16.16)	41 (41.41)	
Osteopenia, n= 89 (%)	38 (42.69)	15 (16.85)	36 (40.44)	
Osteoporosis, n=30 (%)	15 (50)	3 (10)	12 (40)	

*The data were given as a mean ± SD (standard deviation). BMI: body mass index, BMD: bone mineral density

the data revealed that the occurrence of osteoporosis in individuals with diabetes was significantly less when compared the osteoporosis in nondiabetic individuals. However, few studies from Saudi Arabia reported a higher occurrence of osteoporosis in Saudi diabetic patients by 36%, 28%, and 29%, respectively.[14,17] This difference could be explained by the difference in the mean age of the diabetic patients who participated in the study, where our mean age was 65.9 years and their mean age was 56.3 years. Our values are hardly distinguishable from those of Yuhao et al,[18] who estimated the prevalence of osteoporosis in patients with DM in the Chinese population at 37%. Our results have been fully supported by a study carried out on elderly Iranian diabetic patients reported to have markedly high lumbar spine BMD compared to their respective control population without a history of diabetes. In the same Iranian diabetic patients group, no statistical difference was found with those individuals reported to have femoral BMD history. Additionally, the prevalence of osteoporosis was lower in diabetic patients than that in nondiabetic patients.[9] Furthermore, our findings have also been supported by another study on elderly diabetic patients from the UAE, where a higher BMD in DM patients and a lower risk of osteoporosis compared with nondiabetic patients were reported.[19] Moreover, another study supported our novel findings in women, which showed that Arab women with type 2 diabetes had higher spine BMD than women without T2DM.[20] Moreover, our results are consistent with those of the study carried out on Jordanian postmenopausal women with T2DM, which also reported higher BMD levels and a lower risk of osteoporosis as compared with nondiabetic women.[21] On the other hand, our findings contradict those of several other previous studies reported in the literature, suggesting a negative impact of DM on BMD and an increased risk of spine and hip fractures.[22,23] A study of older Chinese females who were not overweight and had T2DM showed that they had lower BMD levels and a higher rate of osteoporosis than women who did not have diabetes.[22] Furthermore, another study carried out on postmenopausal Turkish women showed an insignificant difference in BMD, T-scores, and osteoporosis prevalence in diabetic patients compared to nondiabetic patients.[23] Contrary to our results, a study conducted on Egyptian diabetic

patients showed significantly lower BMD than that in nondiabetic patients.[10] This may be due to the higher incidence of osteopenia. A recent systematic review and meta-analysis showed no relationship between DM and low BMD and insufficient evidence between DM and low bone density.[24] Even though this meta-analysis had a large sample size, it was based on a number of epidemiological case-control studies, so the results still need to be confirmed. Despite conflicting findings in the literature, the differences can be explained by changes in the methods used to measure bone mineral density, differences in the mean age of the population, the mean BMI, the duration and severity of DM, and the type of medications used for diabetes. Low BMD in DM may be related to insulin and insulin-like growth factor deficiency, leading to low bone mass and slow osteoblastic growth.[25] Moreover, the results showed a tendency in the pre-DM and DM groups to have higher BMI values. However, patients with high BMI are at a higher risk of having DM, and several reports found an adverse effect of obesity on bone quality.[26] Other studies recently found an association between excess body fat and osteoporosis.[27] It was expected that high BMI and obesity disturbed the balance of osteoblast and osteoclast activities, resulting in more fragile bones. This effect could be due to the enlargement of adipocytes in the bone marrow and, consequently, the reduction of osteoblasts.[28] Recently, it was found that adipose tissue in bone marrow secretes adipokines that affect the functions of osteoblasts and osteoclasts.[29]

The future implication of the study is very important for diabetic patients as the overall outcomes of this study suggested that the patients with diabetes should be accessed regularly for the risk of onset of osteoporosis but future research are still needed to find out the exact role of osteoporosis in diabetic patients. In this debate, we discussed our findings with other studies performed on various other population, however, it is important for us to mention that individuals with diabetes from different populations have different characteristics, therefore these studies showed different outcomes. Some studies were comparable with our findings whereas other were not.

Study limitations. This study has few limitations such as a retrospective observational study designed, which may not be the ideal for proving a causal association between diabetes and osteoporosis. Moreover, only recruiting patients from a single center could have led to selection bias, which made it impossible to apply the results to the whole of Saudi Arabia. All patients with T2DM should be assessed for osteoporosis risk, and appropriate preventive measures should be provided. Furthermore, prospective, randomized-controlled studies are needed to determine if T2DM is a risk factor for osteoporosis.

In conclusions, this study is from the central region of Saudi Arabia demonstrating that diabetic patients had higher lumbar BMD than nondiabetic individuals. However, femoral BMD was found to be similar in both diabetic and nondiabetic individuals. The data also determined that diabetic patients have a lower osteoporosis risk than nondiabetic subjects. The findings of this study suggested that patients with type 2 diabetes should be regularly assessed for osteoporosis risk and that appropriate preventive measures be provided.

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