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CREATIVE STUDIO

The Prevalence and Risk Factors of Osteoporosis among a Saudi Female Diabetic Population

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Abstract

AIM: This study aimed to assess the prevalence and determinants of osteoporosis [lumbar spine (LS) and femoral neck (FN)] among patients with type 2 diabetes at King Salman Hospital.

MATERIALS AND METHODS: One hundred seventy patients with type 2 diabetes were enrolled in this cross-sectional study in the period from the 1st of January until the 1st of July 2015. Patient selection was based on self-report of the previous diagnosis by a physician, being on an antidiabetic agent, or a fasting glucose of 126 mg/dl as per the American Diabetes Association criteria. A dual energy X-ray absorptiometry scan with the bone mineral density (BMD) categorization based on the WHO cut of levels of T-scores and determination of vitamin D levels were performed. A detailed questionnaire was used to collect demographic data.

RESULTS: Out of 170 participants, 50 (29.4%) were diagnosed as having osteoporosis, while 68 (40%) were diagnosed with osteopenia. Age was determined as a risk factor for a decreased BMD in patients with osteopenia (odds ratio (OR) = 1.1, 95% confidence interval (CI) = (1.0-1.1), p = 0.039) and osteoporosis (OR = 1.1, CI = 1.0-1.2, p < 0.001). Similarly, oral hypoglycemic agents (OHA) increased the risk of decreased BMD in osteopenia (OR = 2.6; CI = 1.0-6.7; p = 0.023) as well as osteoporosis, (OR = 3.8; CI = 1.3-10.9; p = 0.013), while vitamin D deficiency increased the risk of osteopenia OR = 3.0; CI = 1.2-7.2; p = 0.012). Increased BMI decreased the risk of both osteopenia and osteoporosis (OR = 0.9; CI = 0.9-0.99; p = 0.031 vs. OR = 0.9; CI = 0.80-0.95; p = 0.003).

CONCLUSION: Advanced age, OHA and vitamin D deficiency are determinants of decreased BMD in Saudi women with type 2 diabetes, while an increased BMI protects against low BMD.

Introduction

Diabetes mellitus has become a major problem worldwide, and it is speculated that the burden of such a problem will reach 7.7% by the year 2030 [1]. The Arabian Gulf area is one of the most affected regions where the problem of obesity is expected to continue to rise, and five of the region states are likely to be among the ten countries with the highest diabetic morbidity by the year 2030 [1, 2]. Reports about the prevalence of diabetes mellitus in Saudi Arabia estimate the current prevalence to be around 17% with expectations that it will peak at more than 20% by the year 2030 [3].

Osteoporosis is defined by the presence of both reduced bone mass and altered bone quality, along with micro-architectural abnormalities, leading to decreased bone strength and probably pathological fractures [4]. The risk factors for osteoporosis include advanced age, use of glucocorticoids, nutritional factors, low body mass index and genetic factors [5-7]. According to a recent report, more than one-third of the healthy Saudi individuals were found to have osteoporosis [8].

Despite the presence of different reports describing skeletal disorders among patients with diabetes, controversy remains concerning the risk of osteoporosis and its clinical importance among these patients [9]. Some studies have shown osteopenia and frequent bone fractures among type 1 diabetics; nonetheless, evidence demonstrating this risk among type 2 diabetics remains elusive [10,11]. Evidence of high bone mineral density and body mass index (BMI) shown in previous epidemiological studies proposing

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a reduction in fracture risk led to the assumption that type 2 diabetics could have a lower risk of osteoporosis [12]. However, recent evidence suggests that the fracture risk among patients with type 2 diabetes is higher, whether high bone mineral density (BMD) is present or not [10, 13]. Both type 1 and 2 diabetes mellitus is regarded as a risk factor within the Fracture Risk Assessment Tool (FRAX-algorithm), which is commonly used to examine the probability of fracture [14].

The coexistence of osteoporosis and type 2 diabetes mellitus is common among the elderly population, putting this group at higher risk of bone fracture. Additional investigations are desirable to explore possible risk factors and predictors of osteoporosis among elderly.

The aim of the current study was to assess the prevalence and of risk factors for osteoporosis (lumbar spine (LS) and femoral neck (FN) BMD< −2.5 SD T-score) in a cohort of consecutive female patients with type 2 diabetes mellitus.

Patients and Methods

Patients

This is a cross-sectional study where we included a total number of 170 females with type 2 diabetes. The patients were recruited consecutively from the outpatient clinic of King Salman Hospital, Riyadh, Saudi Arabia after obtaining their consent. Data was gathered using a structured questionnaire during the follow-up visits for the control of diabetes between the 1st of January until the 1st of July 2015. The questionnaire included the patients' demographic data, history of comorbidities, medicaments history including vitamin D supplementation and the anti-diabetic agents along with an evaluation of proposed osteoporosis risk factors such as the history of immobility, exercise, and previous fragility fracture.

Methods

The diagnosis of type 2 diabetes was based on reviewing the patients' outpatient clinic medical records of the Department of Internal Medicine, Endocrinology, at King Salman Hospital. The sample size was calculated using the Epi- info statistical calculator utilising the formula

Sample size $n = [DEFF*Np(1-p)]/ [(d^2/Z^2_{1-\alpha/2}*(N-1)+p*(1-p)] = 167$

We used a population size (for finite population correction factor or fpc) (N):1000000, and we assumed that the prevalence of the disease among the Saudi population is 34% based on previous publications, and we calculated our sample size with 5% limit of confidence and an 80% study power.

Diabetes was considered based on self-report of diabetes previously diagnosed by a physician in the medical records, if the patient was already taking antidiabetic medication or by obtaining a fasting glucose reading of126 mg/dl as per the American Diabetes Association criteria [16]. Patients presenting with type 1 diabetes mellitus were excluded from the study. Measurement of BMD was carried at the LS (L2–L4, LS) and the right and left femur necks using dual-energy x-ray absorptiometry (DXA) by a Hologic 4500 bone densitometer. We compared our patient's measurements with age- and sex-matched normal reference values provided by Hologic for Caucasian populations. BMD categorization was based on the cut-off levels of T-scores set by the WHO [where osteoporosis is diagnosed as a (T-score < −2.5 SD), osteopenia (T-score from −1 to −2.5 SD) and normal (t-score > −1 SD)] [17].

Ethical approval

Ethical approval for the current study was obtained from the Ethics Committee of King Fahad Medical city. All participants and patients were enrolled in the study after signing a written informed consent.

Statistical analysis

SPSS for Windows (version 20.0) was used for analysis after data were entered into computer database. To compare the continuous variables (after checking for normality and proportions between the different groups of BMD), one –way ANOVA was used as well as χ^2 tests. Multinomial logistic regression was used when the p value of variables of the one-way ANOVA and χ^2 test were less than < 0.2, with BMD groups entered as the dependent variables and age, body mass index (BMI), history of previous fragility fracture, vitamin D deficiency, history of type 2 diabetes mellitus and use of oral hypoglycemic agents as independent variables. On calculating the odds ratios and 95 % confidence interval, a p value was regarded significant if it is < 0.05.

Results

The general characteristics of the 170 participants are shown in Table 1. Around one-third (29.4%) of our patients were found to have osteoporosis, while 68(40%) of the enrolled women were found to have osteopenia.

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Table 1: Showing the characteristics of the study population

Variable		N = 170 and %
Age in years (mean ± SD)		56.3 ± 8.5
BMI (mean ± SD)		32.2 ± 6.2
Insulin		27 ± 19%
Oral Hypoglycaemics		85 ± 59.9%
Osteoporosis		50 ± 29.4%
Osteopenia		68 ± 40%
Immobility		3 ± 1.8
Exercise		17 ± 10%
Myopathy		18 ± 10.6%
Use of steroids		1 ± 0.6%
Use of Calcium		86 ± 50.6%
Estrogen deficiency		29 ± 17.1%
Smoking		2 ± 1.2%
Early menopause		9 ± 5.3%
Alcohol		0
Rheumatoid Arthritis		0
Vitamin D supplement		84 ± 49.4%
Kyphosis		3 ± 1.8%
Frax score	Low	116 ± 68.2%
	Moderate	34 ± 20%
	High	20 ± 11.8%

Out of the enrolled 170 women, 116 (68.2%) scored low FRAX index, 34 (20%) had intermediate and 20 (11.8%) women a high FRAX index score. Use of oral hypoglycemic medication was confirmed in 59.9% of patients. The prevalence of osteoporosis based on location is shown in Table 2. The comparison regarding the prevalence of osteoporosis between the different groups shows that it is detected more frequently on examining the vertebrae (28%).

Table 2: Prevalence of osteopenia and osteoporosis in postmenopausal diabetic Saudi women according to bone mineral density and WHO criteria

Variable	Normal n (%)	Osteopenia n (%)	Osteoporosis n (%)
Vertebrae	56 (32.9)	66 (38.8)	48 (28.3)
Right femur	114 (67.1)	50 (29.4)	6 (3.5)
Left Femur	115 (67.6)	49 (28.8)	6 (3.5)

While there was no significant difference in the distribution of cases who are on insulin, immobile, those who were exercising, or suffering myopathy, the age, the prior history of fragility fracture, use of oral hypoglycemic agents and vitamin D deficiency were significantly higher in the osteoporosis group compared to the group with normal BMD reflecting that they were risk factors for low BMD. To the contrary, BMD was found to decrease with reductions in BMI (see Table 3).

Table 3: Univariate analysis comparing the characteristics of the study population, between the bone mineral density groups among Saudi women

Variables	Normal (52)	P value	Osteopenia N (68)	P value	Osteoporosis N (50)	P value
Age in years (mean(sd))	52.3 (7)	0.034	56.2 (7. 5)	0.050	60.5 (9.2)	<0.001
BMI(mean(sd))	34.2 (6)	0.040	32.1 (6.1)	0.129	30.2 (6.2)	0.005
Insulin	5	0.351	13	0.110	9	0.278
Oral Hypoglycaemics	33	0.018	34	0.015	18	0.038
Immobility	1	1.000	0	*	2	0.263
Exercise	3	0.872	7	0.475	7	0.381
Myopathy	5	0.093	6	0.762	7	0.641
Vitamin D deficiency	31	0.010	24	0.012	29	0.011
Calcium intake	24	0.015	40	0.012	22	0.010
Use of steroids	0	0.145	0	*	1	0.292
Early Menopause	0	0.999	5	<0.001	4	0.140
Caffeine	15	0.562	0	0.337	0	0.499

*This parameter is set to zero because it is redundant.

Multinomial analyses (Table 4) showed that age was a risk factor for a decreased BMD for both osteopenia (odds ratio (OR) = 1.1, 95% confidence interval (CI) = (1.0-1.1), p = 0.039) and osteoporosis (1.1) (1.0-1.2), p = <0.001). Similarly use of oral hypoglycemic agents increased the risk of decreased BMD in cases with osteopenia (2.6) (1.0-6.7), p = 0.032) as well as with osteoporosis, (3.8) (1.3-10.9), p = 0.013), while vitamin D deficiency increased the risk of osteopenia alone (3.0) (1.3-7.2), p = 0.012).

Table 4: The Odds ratio (95% confidence interval), P value for multinomial analyses where normal bone mineral density was the reference

Variables	Osteopenia (N = 91)				Osteoporosis (N = 55)			
		OR	CI	P value		OR	CI	P value
Age in years (mean ± sd)	56.2 ± 7. 5	1.1	1.0-1.1	3 0.039	60.5 ± 9.2	1.1	1.0-1.2	<0.001
BMI (mean ± sd)	32.1 ± 6.1	0.9	0.9-0.99	0.031	30.2 ± 6.2	0.9	0.80-0.95	0.003
Oral Hypogly-caemics	34	2.6	1.0-6.7	0.023	18	3.8	1.3-10.9	0.013
Vitamin D deficiency	24	3.0	1.2-7.2	0.012	29	1.5	0.5-3.9	0.502

Calcium was set to zero because it was redundant. On the other side high BMI decreased the risk of both osteopenia and osteoporosis (0.9) (0.9-0.99), p = 0.031, 0.9 (0.79-0.95), p = 0.003 respectively.

Discussion

The prevalence of osteoporosis among the diabetic population we studied was 29.4%, which is slightly less than what was previously reported in Saudi Arabia (34%) [8]. This could be explained in the context of what has been described by Vestergaard in his study which showed that patients with type 2 diabetes tend to have a higher BMD. Nonetheless, they have a higher fracture risk [18]. Another important finding reflected by the current study is the agreed upon fact regarding the inverse relation between age and BMD in cases of osteopenia and osteoporosis [19-21] which is likely attributed to the mobilization of calcium from bone. According to the present study, the advancement in age increased the likelihood of osteopenia and osteoporosis with an odds-ratio of 1.1. An explanation for this weak effect is the background of our patients since it is believed that type 2 diabetes is associated with a higher BMD as has been mentioned before. The use of oral hypoglycemic agents was another predictor for the development of osteopenia or osteoporosis as indicated by the current study. Based on our findings, patients on oral hypoglycemic medications have a nearly three times risk of developing osteopenia and more than four times chance of becoming osteoporotic. These findings are in agreement with what was demonstrated by Billington et al. in their

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meta-analysis regarding the effects of thiazolidinediones on BMD [22]. Moreover, it is known that metformin is associated with a higher incidence of bone fractures [23]. It is worth mentioning that our results included oral hypoglycemic agents with no reference to a particular type of the oral hypoglycemic agents. Kumar et al. found that oral hypoglycemic agents did not affect the BMD after usage for three years [24]. The current study showed that BMI protects against a decrease in BMD, such a finding has been claimed by Chen et al. in their study among elderly type 2 diabetic men [25], nonetheless, other researchers declared different findings concerning the relation between BMI and BMD [26].

Expectedly, vitamin D deficiency decreased BMD in diabetic patients we studied, as has been previously shown in another study [27]. In contrast to our findings, Kota et al. found no direct relation between Vitamin D levels and BMD despite showing a significant association with the parathormone levels [28]. However, the effect of vitamin D deficiency was seen in osteopenic patients only, a finding that might be explained by supplementation of some of the osteoporotic patients with vitamin D preparations. We have to acknowledge the fact that more details about the hypoglycemic agents would have led to better conclusions. Including controls would have helped to delineate the type 2 diabetes risk of osteoporosis. One more important limitation to our study is the fact that it has been conducted among a female population and thus it is difficult to extrapolate our results to the whole community.

In conclusion, the current study showed that advanced age, oral hypoglycemic agents and vitamin D deficiency are risk factors for a decreased bone mineral density, while an increased BMI was found to guard against a reduction in BMD in Saudi women. A case-control study on a larger scale is recommended and is expected to describe the risk factors and the relation between type 2 diabetes and osteoporosis in a more clear way.

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