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Increased bone mineral density in postmenopausal women with type 2 diabetes mellitus

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BACKGROUND AND OBJECTIVES: Studies of bone mineral density (BMD) in women with type 2 diabetes mellitus have shown conflicting results. We conducted this study to determine whether postmenopausal women with diabetes have higher BMD than non-diabetic women of similar age, and to investigate the relationship between BMD and relevant clinical characteristics in these groups of women.

PATIENTS AND METHODS: We retrospectively analyzed lumbar spine, femoral neck, and radius BMD data and other relevant clinical data for 130 postmenopausal women with type 2 diabetes mellitus and 166 non-diabetic women collected during a voluntary screening for osteoporosis in postmenopausal women without a history of low bone mass or osteoporotic fractures.

RESULTS: Women with type 2 diabetes mellitus had significantly higher mean lumbar spine BMD (0.903±0.165 vs. 0.824±0.199, respectively, $P<.001$) and mean femoral neck BMD (0.870±0.132 vs. 0.832±0.134, respectively, $P<.05$) than non-diabetic women. In both groups of women, age correlated negatively with BMD levels at all three anatomical sites. Higher body mass index was associated only with higher lumbar spine BMD in both groups. Alkaline phosphatase levels showed a negative correlation with BMD at all sites in women with type 2 diabetes mellitus.

CONCLUSION: Postmenopausal women with type 2 diabetes mellitus have higher BMD levels than non-diabetic women with similar clinical characteristics, and require a more scrutinized approach in managing low bone mass.

Studies on BMD in women with diabetes have conflicting results. Some studies originating from registries in the 1990s showed lower BMD levels in women with both types of diabetes.[1,2] Recent studies have confirmed the deleterius effect of type 1 diabetes on bone density,[3] whereas a normal or even increased BMD was noted in women with type 2 diabetes mellitus.[4] During these analyses, biochemical parameters of calcium and phosphorus metabolism, lipid levels and statin therapy, glycated products levels, lifestyle and body mass index (BMI) were all identified as possible factors in altering BMD in women with type 2 diabetes.[5-7] Several studies explained the results of increased BMD in women with type 2 diabetes by their higher BMI,[8] although some mechanisms resulting from the hyperglycemic state, together with insulin resistance were also noted to improve BMD.[9] We conducted this study to determine whether postmenopausal women with type 2 diabetes mellitus have higher BMD than non-diabetic women of similar age, and to investigate the relationship between BMD and relevant clinical characteristics in these groups of women.

PATIENTS AND METHODS

We retrospectively investigated 130 postmenopausal white women with type 2 diabetes mellitus who underwent dual x-ray bone absorptiometry (DXA) at the outpatient clinic of the Internal Medicine Department of Slavonski Brod General Hospital during a one-year voluntary screening process in our community. Another 166 non-diabetic postmenopausal white women who underwent DXA in the same period were randomly selected as controls from the women who underwent DXA. All studied women had the DXA measurement for the first time, and had no previous history of low bone mass, osteoporosis or osteoporosis therapy.

Exclusion criteria included previously diagnosed osteoporosis, osteoporotic fracture or osteoporosis therapy.

BMD of the lumbar spine, femoral neck and radius using DXA was measured in each patient, and expressed as g/cm^2. All measurements were performed using Hologic QDR 1000 (Texas Instruments), by the same technician involved in the screening process.

The t-test and the Mann-Whitney test were used to investigate the differences in clinical characteristics between the two groups. The differences in BMD of the lumbar spine, femoral neck and radius between diabetic and non-diabetic women were assessed using the t-test. Multiple regression analysis was used to investigate the effect of age, menarche and menopause age, BMI, and laboratory results (serum calcium, phosphorus, alkaline phosphatase, urine calcium and phosphorus, total cholesterol and triglycerides) on lumbar spine, femoral neck and radius BMD in both groups of women. The significance level was set to $P<.05$.

RESULTS

There were no differences between the two groups of women in clinical characteristics, except that women with type 2 diabetes had significantly higher triglycerides (Table 1). Women with type 2 diabetes mellitus had significantly higher mean lumbar spine BMD ($P<.001$) and mean femoral neck BMD ($P<.05$) than non-diabetic women. There were no significant differences between the two groups in the mean radius BMD (Table 2).

In the diabetes group, multiple regression analysis showed a positive correlation of the femoral neck BMD with BMI ($P<.05$), and lumbar spine and radius BMD with menarche age ($P<.05$), while there was a negative correlation of the lumbar spine, femoral neck, and radius BMD with age ($P<.001$) and alkaline phosphatase levels ($P<.05$).

The multiple regression analysis among non-diabetic women revealed a positive correlation of the femoral neck BMD with BMI ($P<.001$) and urine phosphorus ($P<.05$), and a positive correlation of the lumbar spine BMD with menopause age and BMI ($P<.05$). Conversely, there was a negative correlation of the lumbar spine and femoral neck BMD with age ($P<.001$). In addition, femoral neck BMD correlated negatively with serum phosphorus ($P<.05$).

Table 1. Clinical characteristics of the study groups.

Variables	Type 2 diabetes mellitus (n=130)	Non-diabetic (n=166)
Age (years), median (range)	67 (45-80)	67 (41-84)
Menarche age (years), median (range)	14.5 (10-18)	14.5 (11-20)
Menopause age (years), median (range)	49 (30-58)	49 (24-55)
Family history of osteoporosis	4 (3.1%)	5 (3)
Immobility	3 (2.7%)	9 (5.4)
Body mass index (kg/m^2)	29.3±4.5	28.3±4.1
Smoking	15 (11.5%)	16 (9.6)
Milk consumption <500 mL/day	30 (20.1%)	24 (14.5)
Serum calcium (mmol/L)	2.7±0.4	2.4±0.2
Serum phosphorus (mmol/L)	1.1±0.3	1.1±0.6
Serum alkaline phosphatase (U/L)	69.2±22	73.5±26.4
Urine calcium (mmol/L)	5.7±3.2	5.7±3.6
Urine phosphorus (mmol/L)	24.4±15.4	23.9±10.1
Total cholesterol (mmol/L)	6.6±1.5	6.1±1.2
Tryglicerides (mmol/L)	2±1.6*	1.5±0.8

Values are mean±SD unless indicated otherwise. * Significantly higher value than the non-diabetic women (Student's t-test, $P<0.001$)

Table 2. Bone mineral density (BMD) in the study groups.

Measurement site	BMD, mean±SD	
	Type 2 diabetes mellitus	Non-diabetic
Lumbar spine	0.903±0.165*	0.824±0.199
Femoral neck	0.870±0.132†	0.832±0.134
Radius	0.496±0.065	0.485±0.081

* Significantly higher than non-diabetic ($P<.001$). † Significantly higher than non-diabetic ($P<.05$)

DISCUSSION

Women with type 2 diabetes had higher BMD at all three observed sites than non-diabetic women with comparable clinical characteristics. The difference was significant for lumbar spine and femoral neck ($P<.001$ and $P<.05$, respectively), whereas the difference in radius BMD was not significant. Several recent studies in white women reported analogous findings,[4-9] whereas a recent study in an Arabic female population showed osteoporosis to be more common among postmenopausal females with type 2 diabetes.[10] Age and fertility duration were independently correlated with BMD levels. There were no significant differences in BMI between the two groups of women, and the positive correlation between femoral neck BMD and BMI was observed in both groups. Higher BMD in women with diabetes had been attributed to higher BMI,[8] although our results support several findings of higher BMD independent of BMI in women with diabetes.[11] Although the women with type

2 diabetes had similar serum alkaline phosphatase levels to those of women in the control group, we found that their serum alkaline phosphatase levels showed a negative correlation with BMD.[7]

Type 2 diabetes seems to be protective in the process of bone density loss, as we demonstrated in our study. However, an increased fracture risk in women with diabetes was reported in many studies, and was attributed mainly to neurological and visual complications that facilitate fall accidents, or low bone quality.[12] Today, there are sufficient data that support the concept of preserved bone density in hyperinsulinemia, thus the increased fracture risk in women with type 2 diabetes could also be explained by altering processes in new bone formation and bone microarchitectural integrity in the hyperglycemic state.[12]

The limitation of our study was the cross sectional design, and the inability to compare fracture risk between the observed groups, since fractures represent the most important aspect of osteoporosis. Fracture risk analyses require a higher number of patients from standardized registries, which does not exist in our clinical settings. It would be also interesting to assess the relationship between the duration of diabetes, and levels of glycation products with both BMD and fracture risk. Some studies showed that good glycemic control prevents bone loss in both types of diabetes, explaining normal BMD levels in type 2 diabetes with better glycemic control.[13,14] Our study could not show differences in BMD levels among women in relation to glycemic control.

We conclude that osteoporosis in women with type 2 diabetes needs a more scrutinized approach because BMD levels in diabetic women may not be sufficient in identifying those at risk for fractures, knowing that substantial evidence exists of their increased fracture risk. A better understanding of diabetes and osteoporosis may help preventing fractures in the growing population of post-menopausal women with type 2 diabetes mellitus.

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