Osteoporosis and Osteoporotic Fractures in Postmenopausal Women with Type 2 Diabetes Compared with Non-Diabetic Cases

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Abstract

Objective: Correlation of osteoporosis (OP) with type 2diabetes mellitus (DM) is not as clear as type 1 DM. The purpose of this study was to compare the frequency of OP and osteoporotic fractures in post- menopausal women with and without type 2 DM in Sari, Iran.

Materials and Methods: Eighty post-menopausal women with type 2 DM and 80 non-diabetic controls enrolled in this study. Bone mineral density was determined with dual energy X-ray absoptiometry of L2-L4 in spine and femoral neck. Vertebral fracture was reported by a radiologist on thoraco-lumbar x ray. Hip and wrist fractures were determined by patients self-report and ascertained by radiographs. T test, X^2 and Fisher's exact tests were used for data analysis.

Results: The mean age of diabetic women with and without osteoporosis was 69±2.7 and 69.3±5 years, respectively (p=0.01). Diabetes duration, HbA1C and BMI were not statistically different between two groups. Diabetic complications and anti-diabetic agents, or age and duration of diabetes were not different in diabetic patients with OP or osteoporotic fracture.
The mean of T-score in lumbar spine was -1.65±1.3 in diabetics and -2.11±1.3 in controls (p=0.03). T-score in femoral neck was not significantly different. In diabetic patients, the prevalence of osteoporosis was 27.5% at lumbar spine and 17.5% at femoral neck and in controls were 46.3% and 27.5%, respectively (p=0.04 and 0.1). Fractures were less common in diabetics (18.8% vs. 32.5%, p=0.04).

Conclusion: This study showed that osteoporosis and osteoporotic fractures is less common in post-menopausal diabetic women compared to non-diabetic subjects.

Key Words: Osteoporosis, Fractures, Type 2 Diabetes

Introduction

Diabetes Mellitus(DM) prevalence is estimated 6-8% in worldwide (1). DM and osteoporosis (OP) are chronic diseases with high incidence in old population (2). Osteoporosis is a preventable and treatable disease that is usually asymptomatic until a

fracture occurs. The risk of osteoporosis in patients with type 2 DM is not as clear as type 1. Bone can be affected by DM through multiple mechanisms including obesity, insulin effects, advanced glycosylation end products accumulation in collagen, hypercalciuria, impared renal function, low insulin-like growth factor-I, microangiopathy, and inflammation (3). Leptin also may have a role in regulation of osteoblast function and bone mass in type 2 diabetes mellitus (4).

Longer duration of DM, low body mass index (BMI) and old age have been suggested as osteoporosis risk factors in diabetics, but correlation between osteoporosis and glycemic control has not been confirmed (5, 6).

There are some controversies about the relationship between type 2 DM and OP and fractures. It is believed that despite higher bone density in femoral neck and spine, diabetic women have lower femoral neck strength and are at greater risk of fractures (7, 8). Elderly diabetics have an increased risk of falls, because of poor vision, peripheral neuropathy, and weak muscular performance (3)

Older age, more duration of disease, presence of diabetic retinopathy and neuropathy, and previous fracture were correlated with fractures in diabetic patients (5, 6, 9). There are some reports about the effects of anti-diabetic drugs on bone tissue and association with bone fracture (10-12). Some studies suggested that metformin has a direct effect on bone tissue by reducing advanced glycosylation end products accumulation, whereas insulin by directly acting on osteoclast activity and thiazolidinediones (TZD) leads to unbalanced bone remodeling by switching the mesenchymal progenitor cells maturation to adipose rather than bone tissue (10, 11).

The purpose of this study was to compare the frequency of OP and osteoporotic fractures in post-menopausal women with and without type 2 DM in Sari, Iran.

Materials and Methods

Eighty post-menopausal women with type 2 DM were compared with 80 non-diabetic women as controls. Diabetic patients were selected from DM health care in Sari, Iran, during 2010-2011. Menopausal women aged ≥ 65 years with any menopause period or aged ≥ 60 years with more than 10 years menopause period included in the study. All patients were evaluated by an endocrinologist in order to exclude endocrine disorders (such as Cushing disease, hypopituitarism, hyperthyroidism, hyperparathyroidism, and amenorrhea before age 40 year).Other exclusion criteria were inflammatory rheumatologic disorders, renal or liver failure and usage of such drugs as anti-epileptics, glucocorticoids and hormone replacement therapy (HRT). Patients with BMI≤18.5 or ≥40 were excluded as well.

Data about duration of diabetes mellitus, glucose lowering drugs (insulin or oral hypoglycemic agents), level of glycosylated hemoglobin (HbA1C) and diabetes complications such as nephropathy, neuropathy and retinopathy were recorded for diabetic patients. Retinopathy was detected by an ophthalmologist and subjects suffering from albiminuria (micro or macro) were considered as nephropathic.

Other factors that potentially influenced BMD such as cigarette smoking, sun light exposure more than 15 minutes/day, walking more than 30 minutes/day and BMI were recorded as well.

BMD was done for all subjects by dual energy x-ray absorptiometry method (DEXA). (Hologic- discovery, USA) in spine and hip regions. AP and lateral thoracolumbar X-rays also were obtained in all patients. A vertebral fracture was diagnosed if 20% or more height reduction was observed by a radiologist that was blinded tothe patient group and BMD results (13). Serum calcium, phosphorus, alkaline phosphates and 24- hour urine calcium were measured. OP was defined as T-score ≤ -2.5 and osteopenia as T-score between -1.0 and -2.5. Osteoporotic fracture or fragility fracture was defined as fracture that had occurred following a fall from standing height or less or with no trauma (14).

The SPSS software was used for statistical analysis. Independent samplest test was used for quantitative, and X^2 and Fisher's exact test

for qualitative variables. Odds ratio was calculated for estimation of probable risk factors. The study was approved by the Mazandaran University of Medical Sciences Ethics Committee, and an informed consent was obtained from all participants.

Results

In this study, 80 diabetic and 80 non- diabetic postmenopausal women were compared. The mean age was 68.66±4.8 and 68.86±6.7 years in case and control group, respectively (p=0.8). The mean duration of menopause was 20.82±9.44 years in diabetic group and 21.42±8.70 years in control group (p=0.7) (Table 1).

3.8% of cases and 6.3% in control group were smokers (p=0.7).Sun exposure more than 15 minutes per day was 47.5% and 43.8% in diabetics and controls, respectively (p=0.5). The mean of spinal T score in diabetics was statistically higher than control group (P=0.03). Osteoporosis was diagnosed in 27.5% of diabetic subjects at lumbar spine and 17.5% at hip site; in non-diabetics this was 46.3% and 27.5%, respectively (p=0.04 and 0.1).

The mean of spinal Z- score was 0.03±1.2 and -0.56±1.3 in cases and controls, respectively (p=0.003). Hip T-score and Z- score were not statistically different between two groups (Table1) .In diabetic patients, 39 cases (%48.8) were osteoporotic and 24 cases (%30) were osteopenic. The prevalence of osteoporosis and osteopenia was 62.5% and 25% in cases and controls, respectively (p=0.2). Fractures were less common in diabetics than non-diabetics (18.8% vs. 32.5%, p=0.04). Fractures according to sites of involvement are shown in Table 2.

Retinopathy and nephropathy were seen in 31.3% and 22.5% of diabetic women and fifty percent of them suffered from neuropathy. Osteoporotic and non-osteoporotic (normal

Table1- Basic quantitative data in diabetic and non-diabetic postmenopausal women in Sari, Iran

Variables	Diabetic women Mean± SD	Non-diabetic women Mean± SD	P value
Age(year)	68.66±4.8	68.86±6.6	0.8
Weight(kg)	68.42±10.5	67.61±11.00	0.6
Menopause duration (year)	20.82±9.4	21.42±8.70	0.7
Ca(mg/dl)	9.39±0.5	9.39±0.5	0.9
P(mg/dl)	3.93±0.6	3.64±0.6	0.002
Alp(u/l)	174.26±94.2	179.83±55.2	0.7
Urine Ca(mg/day)	143.93±81.3	124.47±75.7	0.1
BMI(kg/m^2)	29.62±4.5	28.38±4.2	0.08
Spinal T score	-1.65±1.3	-2.11±1.3	0.03
Spinal Z score	0.03±1.2	-0.56±1.3	0.003
Femur T score	-1.51±1.1	-1.69±1.3	0.3
Femur Z score	0.14±0.90	-0.13±0.90	0.08

Table 2- Osteoporotic fractures in diabetic and non-diabetic postmenopausal women in Sari, Iran

Site of fracture	Diabetics (N & %)	Non-diabetics (N & %)	P Value
Thoracolumbar	14 (17.5%)	19 (23.8%)	0.33
Hip	0(0%)	3 (3.8%)	0.08
Wrist	1 (1.2%)	5 (6.2%)	0.09
Total	15(18.8%)	26(32.5%)*	0.04

***one subject had both wrist and hip fractures**

BMD and osteopenia) diabetic women were compared with each other. Osteoporotic diabetic women were older (69±2.7 vs. 69.3±5 years, p=0.01).Diabetes duration, HbA1C and BMI were not statistically different between two groups(29.5±4.6 vs. 29.7±4.3, p=0.3). Diabetic complications and consumption of oral hypoglycemic agents or insulin therapy were not statistically different between osteoporotic and non-osteoporotic diabetic women. Osteoporotic fracture was detected in 28.2% of diabetic subjects with osteoporosis and 14.6% in non-osteoporotic diabetic women (p=0.1). The osteoporotic fracture in control group with and without osteoporosis was 44% and 26.7%, respectively (p=0.1).

The mean age of diabetic women with and without osteoporotic fracture was 67.7± 4.4 and 68.9±4.9 years (p=0.4) and duration of diabetes was 11.54±4.4 and 10.49±8.4 years, respectively (p=0.7). Osteoporotic fractures did not have association with diabetes complications or hypoglycemic agents.

Discussion

The results of this study showed that postmenopausal women with type 2 diabetes mellitus have a better BMD and lower incidence of bone fractures. Overall, osteoporosis was detected in 48.8% and 62.5% of diabetic and non-diabetic postmenopausal women, respectively. Lumbar spine osteoporosis was less common in diabetic group than controls. Frequency of fractures was less in diabetic group as well. The prevalence of osteoporosis in diabetic and non-diabetic postmenopausal women was 48.8% and 62.5%, respectively. The most prevalent site of fractures was thoracolumbar vertebrae (17.5%). In our study glucose lowering drugs including insulin and oral hypoglycemic agents and also DM complications didn't correlate with osteoporosis or osteoporotic fractures in postmenopausal diabetic women.

Our results support the findings of some previous studies. In one study in California, type 2 diabetic women had better BMD than women with normal glucose tolerance (15) and according to report of another study in China on 1042 post-menopausal type 2 diabetic women and 919 non-diabetics, postmenopausal women with type 2 DM had higher BMD and lower lumbar spine fractures (16). The researchers in Spain evaluated 111 patients with type 2 DM and concluded that in obese postmenopausal Caucasian women, type 2 DM is correlated with higher BMD score in lumbar spine (17).

Our results were different with some other studies. BMD findings in 206 postmenopausal Turkish women with type 2 diabetes compared to 61 age-matched postmenopausal non-diabetic women were not different (6) and in a large cohort study in North Carolina, USA, women with diabetes mellitus though had higher hip and spine BMD score, but they were at higher risk of fractures (8). In one study in Denmark by Vestergaard, type 2 DM was associated with more fractures in hip and forearm (13) and this author in another study showed that diabetes mellitus and its complications were associated with higher risk of fractures (18).

In the present study, HbA1C and anti-diabetic drugs including insulin and oral hypoglycemic agents and diabetes complications were not correlated with osteoporosis or fractures in diabetic women. There are some data about correlation between anti-diabetic agents and BMD and fracture. Insulin (9) and thiazolidinediones (10,19)were introduced as fracture risk factors and also insulin(10), metformin (10,13) and sulfonylurea (13) were suggested as protective factors. According to previous studies, there are some controversies about the role of glycemic control in prevention of osteoporosis. Some studies suggested a protective role (5,6) and others did not agree(20). The difference of these studies may be due to different races, BMI, cultures, nutrition, life style, medical care and some other unknown confounders. Diabetes mellitus complications were suggested as osteoporosis or fractures risk factors (5,6,9) but we didn't find correlation between them .It may be due to small sample size in our study. The serum phosphate level was lower in control group than diabetic women in our study. It may be due to vitamin D deficiency that is highly

prevalent in north of Iran (21). The limitations of our study were small sample size and no measurement of serum vitamin D level.

Conclusion

In this study, osteoporosis and osteoporotic fractures were less common in post-menopausal diabetic women than non-diabetic subjects. We can conclude that type 2 diabetes mellitus is not an independent risk factor for osteoporosis or osteoporotic fractures at least in our population.

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