Osteoporosis in Postmenopausal Diabetic Women; Prevalence and Related Factors

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ABSTRACT

Introduction: Diabetes mellitus and osteoporosis are two frequent medical conditions with an increasing prevalence in elderly. This study is conducted to evaluate osteoporosis in postmenopausal females with type 2 diabetes mellitus in Sanandaj, the provincial center of Kurdistan province in the west of Iran.

Methods: From an initial population of 2500 women with type 2 diabetes, 242 postmenopausal women were randomly selected and were compared with 221 non-diabetic postmenopausal women, matched by age and body mass index (BMI). Bone mineral density (BMD) was measured at the L2–L4 vertebrae (anteroposterior projection) and femoral neck with dual energy X-ray absorptiometry (DXA). The statistical significance was set at a P value of .05 or lower.

Results: Prevalence of femoral neck osteoporosis in diabetic women was 30.2 percent (73 cases) and osteopenia was 48.3 percent (117 cases). Osteoporosis prevalence in spine was 7.9 percent (19 cases) and ostropenia was 46.3 percent (112 cases). Osteoporosis in both femoral neck (P=0.001) and spine (P=0.04) were significantly higher in patients than in controls. Correlation between HbA1c and femoral neck (p=0.11, correlation coefficient=0.04) and also spine (p=0.10, correlation coefficient= -0.12) T score was not significant. No significant correlation was found between osteoporosis with presence of microalbuminuria (P=0.91), retinopathy (P=0.33), hypertension (P=0.70), ischemic heart disease (P=0.57) and insulin therapy (P=0.08).

Conclusion: This study shows that type 2 diabetic patients have significantly lower T score values and more frequency of osteoporosis than healthy postmenopausal women.

Key Words: Osteoporosis, Type 2 diabetes, Postmenopausal, BMD

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INTRODUCTION

Osteoporosis is a silent epidemic that constitutes a great socio-economic problem, with a negative impact both on morbidity and mortality (1, 2). It is a bone condition defined by low bone mass, increased fragility, decreased bone quality, and an increased fracture risk. It is the most prevalent metabolic bone disease in the world (3, 4). It is not symptomatic until there is a pathologic fracture. Thus, the true occurrence of osteoporosis may be significantly underestimated because many women who suffer minimal trauma fractures still are not being evaluated for osteoporosis (5, 6). To this point identifying and evaluating populations at increased risk of developing osteoporosis is critical to disease prevention and management. The extension of the average life expectancy of people with diabetes has increased its prevalence in older age, and it is projected that by the year 2025, the majority of persons with diabetes will be aged 65 years or older (7). This fact has increased the significance of osteoporosis in such patients. Although osteoporosis traditionally has not been listed as a complication of diabetes, some of anecdotal studies were suggested possible increased risk of osteoporosis in patients with either type 1 or type 2 diabetes (8, 9).

The association between diabetes mellitus and osteoporosis remains controversial (9). Although the metabolic abnormalities of diabetes potentially affect bone metabolism, structure and mineral density it is not clear if these changes are associated with a significant increase in fracture risk (10-12).

The study was conducted to evaluate osteoporosis in postmenopausal females with type 2 diabetes mellitus in Sanandaj, the provincial center of Kurdistan province in the western of Iran in the summer 2007.

METHODS

Subjects:
In the study post menopausal diabetic women were compared with non-diabetic women for osteoporosis. The diabetic patients were derived from the Diabetes Outpatient Clinic belonging to our department. From an initial population of 2500 women with type 2 diabetes, 242 post menopausal women were randomly selected and studied. The inclusion criteria for this study were having been diagnosed with type 2 diabetes and having lived with the disease for more than 2 years.

Control group, featuring 221 non-diabetic post menopausal women, were matched by age and body mass index (BMI). Exclusion criteria for all women were the presence of any disease or use of medication (including hormone replacement therapy) that has a known influence on bone metabolism and restricted daily activity.

Study protocol was reviewed and approved by local committee of ethics in Kurdistan University of Medical Sciences.

Clinical assessment:
All patients completed a comprehensive questionnaire inquiring about their medical and lifestyle characteristics (i.e., menopausal status, parity, duration of diabetes, comorbidities, frequency of hospital admissions, details of past fractures, as well as alcohol and cigarette smoking habits). Body weight was measured in light clothing and without shoes, whereas BMI was calculated by dividing weight in kilograms by height in square meters.

HbA1c was measured using an automated HPLC analyzer. Microalbuminuria was taken as urinary albumin excretion exceeding 30 mg/dl on a 24-h urine sample when two of three tests were positive after the exclusion of urinary tract infection, uncontrolled hypertension, and heart failure. A subject was considered as having retinopathy if any grade of retinopathy was detected by ophthalmoscopy. Cerebrovascular disease status was reported from prior hospitalizations. A patient was classified as having coronary artery disease (CAD) if there was a history of angina, myocardial infarction, angioplasty, coronary

artery bypass grafting, and/or definite myocardial infarction found on an electrocardiogram.

Bone density measurements:
BMD was measured at the L2–L4 vertebrae (anteroposterior projection) and femoral neck with dual energy X-ray absorptiometry (DXA), using the Norland XR- 46 densitometer (Manufactiuring: 2002, Norland medical systems, INC USA). Estimation of the frequency of osteopenia or osteoporosis was based on the T score value, which represents the standard deviations of the individual BMD value from the BMD value of young sex-matched normal people(13).

The WHO's operating definitions of osteopenia and osteoporosis are, respectively, bone density between 1 and 2.5 standard deviations below the mean value and bone density 2.5 standard deviations below the mean value for young adult White women at the lumbar spine (L1– L4), total hip, femoral neck, and radius based on T scores (14).

Statistical analysis:
Results are expressed as mean ± S.D. values and as percentages for the qualitative variables. The differences were tested by Student's t test, Chi- sqaure or the nonparametric Mann– Whitney U test as appropriate. Multiple linear regression analysis was used to assess the relationship between BMD and affecting parameters. Because BMI and calcium intake are known to be correlated with change in BMD from previous studies, general linear modeling was used to compare BMD between the type 2 diabetes and control groups after adjusting for these variables. The statistical significance was set at a P value of 0.05 or lower.

RESULTS

We analyzed the data of 242 patients with diabetes mellitus and 225 subjects as control group. Table 1 shows clinical and laboratory characteristics of diabetic patients. In Table 2 diabetic patients were compared with control group.

Table 1: Demographic, clinical and laboratory characteristics of diabetic women (n=242)

Diabetes Variable	Distribution
Age at diagnosis (years ± S.D)	43.2 ± 7.8
Symptom of hyperglycemia at diagnosis	41 (16.94%)
Duration of diabetes (years ± S.D)	5.9 ± 3.7
HbA1c %	8.1 ± 1.9
Insulin therapy	40 (16.5%)
Hypertension	137 (56.6%)
Retinopathy	38 (15.7%)
Microalbuminuria	33 (13.6)
Ischemic heart disease	19 (7.8%)

Table 2: Comparison of type 2 diabetic women with control subjects

Characteristics	Diabetics (N=242)	Control (N=225)	P Value
Age (years ± S.D)	53.6 ± 10.59	54.0 ± 8.0	0.59
Age at menopause (years ± S.D)	45.8 ± 4.9	47.1 ± 5.4	0.29
BMI (kg/m2, mean ± S.D)	28.6 ± 6.1	27.5 ± 5.7	0.45
Current smoker	21	14	0.31
Alcohol drinker	0	0	-

Table 3: Comparison of T score and BMD between tow groups

	Diabetics (N=242)	Control (N=225)	P Value
Femoral neck T score	-1.82 ± 1.18	-1.48 ± 1.12	0.002
Total spine T score (L2–L4)	-1.01 ± 1.06	-1.12 ± 0.88	0.20
Femoral neck osteoporosis*	73 (30.2%)	39 (17.3%)	0.001
			OR=2.06 (1.30 - 3.28)
Lumbar osteoporosis*	19 (7.9%)	14 (6.2%)	0.04
			OR=2.15 (0.94 - 4.99)
Femoral neck osteoporosis and osteopenia*	190 (78.5%)	162 (72.0%)	0.10
Lumbar osteoporosis and osteopenia*			
	131 (54.1%)	14 (6.2%)	0.09

* Frequency according to T score

Prevalence of femoral neck osteoporosis in diabetic women was 30.2 percent (73 cases) and osteopenia was 48.3 percent (117 cases). Osteoporosis prevalence in spine was 7.9 percent (19 cases) and ostropenia was 46.3 percent (112 cases). Osteoporosis in both femoral neck and spine were significantly higher in cases than in controls (Table 3). Correlation between HbA1c and femoral neck (p=0.11, correlation coefficient=0.04) and also spine (p=0.10, correlation coefficient= -0.12) T score was not significant. No significant correlation was found between osteoporosis with presence of microalbuminuria (P=0.91), retinopathy (P=0.33), hypertension (P=0.70), ischemic heart disease (P=0.57) and insulin therapy (P=0.08).

DISCUSSION

According to the results of this study, osteoporosis in femoral neck (OR=2.06, CI 1.30 - 3.28, P=0.001) and spine (OR=2.15, CI=0.94-4.99, P=0.04) were significantly more prevalent in diabetic women in

comparison to control subjects, however mean femoral neck T score was lower in patients (p=0.002) it was not significant in supine (0.20).

Some studies have investigated effects of type 2 diabetes on bone mass in comparison to type 1 diabetes. However, the findings are inconsistent. Authors have reported lower, equal and greater bone mass in people with type 2 diabetes relative to diabetes-free control subjects (15-18). This persistent controversy is probably largely related to the complex pathophysiology of type 2 diabetes and the vast differences in study designs, BMD measurement technology, examination of BMDs at different sites, selection of patients, and presence or absence of complications.

High frequency of osteoporosis among post menopausal diabetic women in our study may be as a consequence of lower socioeconomic level, scant sun exposure, low calcium diet, lack of hormone replacement therapy or use of other medications to prevent osteoporosis.

The different insulin levels in type 2 diabetic patients, high in new-onset cases and low in long-standing cases, might be one of the explanations for the contradictory results of previous studies (19). Previous studies showed a positive correlation of insulin levels with BMD because insulin has an anabolic effect on bone (20). Moreover, there are reports that imply an effect of insulin on cortical bone that is different from its effect on cancellous bone (21).

Two studies found that individuals with type 2 diabetes had lower bone density relative to nondiabetic control subjects (15, 22). However, one (15) examined people who were using insulin to control their diabetes, whereas the other study (22) examined patients using dietary or oral diabetes agents. Two other studies found no difference in bone density between type 2 diabetic patients and control subjects (23, 24), but they had limited sample size (47 and 19, respectively); therefore, findings may not be applicable to other studies or

have suffered from low statistical power. Authors of one study which was published recently, concluded postmenopausal women with type 2 diabetes mellitus have higher BMD levels than non-diabetic women with similar clinical characteristics (25).

In the present study, mean age of diabetic women was 53.6 ± 10.59 which is at least 10-12 years younger than previous studies. This point may explain the effect of type 2 diabetes mellitus on osteopenia and osteoporosis more relevant because osteoporosis in older age could be related to duration of menopause and hormonal deprivation.

CONCLUSION

In conclusion, this study shows that type 2 diabetic patients have significantly lower T score values and more frequent osteoporosis than healthy postmenopausal women.

REFERENCES

1. Hadjidakis DJ, Mylonakis AM, Sfakianakis ME, Raptis AE, Raptis SA. Diabetes and premature menopause: is their co-existence detrimental to the skeleton? Eur J Endocrinol 2005; 152(3):437-442.
2. Reyes Balaguer J, Moreno Olmos J. Prevalence of osteopenia and osteoporosis in postmenopausal women. Aten Primaria 2005; 35(7):342-345.
3. Phillips P, Braddon J. Osteoporosis--diagnosis, treatment and management. Aust Fam Physician 2004; 33(3):111-119.
4. Zylstra RG, Porter LL, Shapiro JL, Prater CD. Prevalence of osteoporosis in community-dwelling individuals with intellectual and/or developmental disabilities. J Am Med Dir Assoc 2008; 9(2):109-113.
5. Siris ES, Miller PD, Barrett-Connor E, Faulkner KG, Wehren LE, Abbott TA et al. Identification and fracture outcomes of undiagnosed low bone mineral density in postmenopausal women: results from the national osteoporosis risk assessment. JAMA 2001; 286(22):2815-2822.
6. Guardia G, Parikh N, Eskridge T, Phillips E, Divine G, Rao DS. Prevalence of vitamin D depletion among subjects seeking advice on

osteoporosis: a five-year cross-sectional study with public health implications. Osteoporos Int 2008; 19(1):13-19.

7. Boyle JP, Honeycutt AA, Narayan KM, Hoerger TJ, Geiss LS, Chen H et al. Projection of diabetes burden through 2050: impact of changing demography and disease prevalence in the U.S. Diabetes Care 2001; 24(11):1936-1940.

8. Chau DL, Edelman SV. Osteoporosis and Diabetes. Clin Diabetes 2002; 20:153-157.

9. Räkel A, Sheehy O, Rahme E, LeLorier J. Osteoporosis among patients with type 1 and type 2 diabetes. Diabetes Metab 2008; 34(3):193-205.

10. Chau DL, Edelman SV, Chandran M. Osteoporosis and diabetes. Curr Diab Rep 2003; 3:37-42.

11. Dominguez LJ, Muratore M, Quarta E, Zagone G, Barbagallo M. Osteoporosis and diabetes. Reumatismo 2004; 56:235-241.

12. Inaba M. Secondary osteoporosis: thyrotoxicosis, rheumatoid arthritis, and diabetes mellitus. J Bone Miner Metab 2004; 22(4):287-292.

13. Robitaille J, Yoon PW, Moore CA, Liu T, Irizarry-Delacruz M, Looker AC et al. Prevalence, family history, and prevention of reported osteoporosis in U.S. women. Am J Prev Med 2008; 35(1):47-54.

14. Fujiwara S. Difference in prevalence of osteoporosis diagnosis by bone density measurement within various bone sites. Nippon Rinsho 2007; 65 (Suppl 9):117-120.

15. Isaia G, Bodrato L, Carlevatto V, Mussetta M, Salamano G, Molinatti GM. Osteoporosis in type II diabetes. Acta Diabetol Lat 1987; 24:305-310.

16. Yamaguchi T, Sugimoto T. Calcium homeostasis and osteoporosis in diabetes mellitus and the metabolic syndrome. Clin Calcium 2008; 18(7):904-911.

17. Vuksanovic M, Durica S, Zerajic B. Diabetes mellitus--a risk factor for the development of osteoporosis. Vojnosanit Pregl 2008; 65(9):692-698.

18. Rehorkova P. Metabolic bone diseases and diabetes. Vnitr Lek 2006 ;52(5):485-487.

19. Stolk RP, Van Daele PL, Pols HA, Burger H, Hofman A, Birkenhäger JC et al. Hyperinsulinemia and bone mineral density in an elderly population: The Rotterdam Study. Bone 1996; 18(6):545-549.

20. Yano H, Ohya K, Amagasa T. Insulin enhancement of in vitro wound healing in fetal rat parietal bones. J Oral Maxillofac Surg 1996; 54(2):182-186.

21. Majima T, Komatsu Y, Yamada T, Koike Y, Shigemoto M, Takagi C et al. Decreased bone mineral density at the distal radius, but not at the lumbar spine or the femoral neck, in Japanese type 2 diabetic patients. Osteoporos Int 2005; 16:907-913.

22. Haffner SM, Bauer RL. The association of obesity and glucose and insulin concentrations with bone density in premenopausal and postmenopausal women. Metabolism 1993; 42(6):735-738.

23. Sosa M, Dominguez M, Navarro MC, Segarra MC, Hernández D, de Pablos P et al. Bone mineral metabolism is normal in non-insulin-dependent diabetes mellitus. J Diabetes Complicat 1996; 10(4):201-205.

24. Avery L. Diabetes mellitus types 1 and 2: an overview. Nurs Stand 1998; 13(8):35-38.

25. Hadzibegovic I, Miskic B, Cosic V, Prvulovic D, Bistrovic D. Increased bone mineral density in postmenopausal women with type 2 diabetes mellitus. Ann Saudi Med 2008; 28(2):102-104.