

## The Relationship Between Type 2 Diabetes Mellitus and Osteoporosis in Elderly People: a Cross-sectional Study

Mohammad Ali Bayani<sup>1</sup>, Ahmad Karkhah<sup>2</sup>, Seyed Reza Hoseini<sup>3\*</sup>, Roya Qarouei<sup>4</sup>, Haji Qorban Nourodini<sup>5</sup>, Ali Bijani<sup>6</sup>, Robert G Cumming<sup>7</sup>

1. Department of Internal Medicine, Ayatollah Rouhani Hospital, Social Determinants of Health (SDH) Research Center, Babol University of Medical Sciences, Babol, Iran.

2. Cellular & Molecular Biology Research Center, Health Research Institute, Student Research Committee, School of Medicine, Babol University of Medical Sciences, Babol, Iran.

3. Department of Community Medicine, Social Determinants of Health(SDH) Research Centre, Babol University of Medical Sciences, Babol, Iran.

4. General practitioner, Babol University of Medical Sciences, Babol, Iran.

5. Department of Radiology, Babol University of Medical Sciences, Babol, Iran.

6. Social Determinants of Health (SDH) Research Center, Babol University of Medical Sciences, Babol, Iran.

7. School of Public Health, University of Sydney, New South Wales, Australia.

Submitted 17 Jul 2016; Accepted 21 Aug 2016; Published 06 Oct 2016

Diabetes mellitus (DM) and osteoporosis are common diseases and their prevalence increases with age. Several investigations have indicated that type 1 DM has a significant relationship with bone loss, whereas in type 2 diabetes, this relationship is controversial. Therefore, this study was conducted to determine the relationship between osteoporosis and type 2 DM in elderly people. This population-based study had been carried out on 1151 elderly people in Amirkola, northern Iran. L2-L4 lumbar spine bone mass and the left femoral neck density were measured by dual-energy X-ray absorptiometry (DEXA). In addition, diagnosis of diabetes was done by measuring fasting blood sugar (twice times FBS  $\geq$  126 mg/dl), according to the WHO criteria or self-reported as well as based on a doctor's prescription. Of total, 362 (31.45%) of patients had DM. The average age of diabetic patients was  $68.9 \pm 6.93$  years and in non-diabetic group was  $68.68 \pm 7.09$  years ( $P = 0.18$ ). The mean L2-L4 lumbar spine bone mass in the diabetic group was  $0.90 \pm 0.19$  g/cm<sup>2</sup> and in the non-diabetic group was  $0.85 \pm 0.18$  g/cm<sup>2</sup> ( $P = 0.001$ ). The mean lumbar bone mineral density was higher ( $P = 0.0001$ ) in diabetic men than in non-diabetic men, as well as in women ( $P = 0.0001$ ). In addition, the mean femoral neck density in diabetic group was  $0.85 \pm 0.16$  g/cm<sup>2</sup> and in the non-diabetic group was  $0.84 \pm 0.15$  g/cm<sup>2</sup> ( $P = 0.48$ ). Moreover, the femoral neck bone mineral density in diabetic men was higher than in non-diabetics ( $P = 0.03$ ), whereas in diabetic and non-diabetic women, there was no significant difference ( $P = 0.52$ ). Our results demonstrated that the mean lumbar and femur bone mineral densities in older people with type 2 DM was higher than people without DM.

**Key words:** Type 2 diabetes mellitus, osteoporosis, bone mineral density

\*Correspondence: Department of Community Medicine, Social Determinants of Health (SDH) Research Centre, Babol University of Medical Sciences, Babol, Iran. E-mail: hosseinirezayeh@gmail.com

Decreased bone density and reduction in the bone strength are most common metabolic bone problems, which are usually diagnosed after bone fractures, especially in the femoral neck and lumbar spine. The incidence of these fractures in USA is 3.1 million cases and also 20% of all deaths result from hip fractures (1). In addition to aging and menopause which are known risk factors for osteoporosis, other factors could also act as a risk factor for osteoporosis, including diabetes mellitus (DM) (2). Several reports indicated that type 1 DM has a strong relationship with osteoporosis (2-4); whereas in the case of the relationship between type 2 diabetes and osteoporosis, there has been inconsistency in the studies (5, 6). In some studies, people with type 2 diabetes had a higher bone mineral density (BMD) than the control group (6, 7). However, some other studies have not found significant differences (5, 8). The results of a study in Saudi Arabia revealed higher prevalence of osteoporosis in postmenopausal diabetic women compared to normal women (9). In addition, in Rotterdam study, men and women with type 2 diabetes had higher BMD and a lower risk for non-vertebral (6). Moreover, obtained results from Health ABC study demonstrated that people with type 2 diabetes had higher BMD at the hip area (10). Shahin et al. showed that BMD in the lumbar spine and femur was higher in diabetic patients than normal people (11). Given the controversies in the above-mentioned studies, this study aimed to determine the relationship between BMD and type 2 DM in elderly people aged 60 years and over.

## Materials and methods

### Study population

This study is a part of a comprehensive cohort study entitled Amirkola Health and Ageing Project (AHAP) (No. 892917), which has been in progress since 2011 on all 60 years and over

population of Amirkola located in north of Iran (12). The elderly were invited to participate in the study through letters and phone calls providing the necessary information about the project. Among 2234 elderly people in Amirkola, 1616 people have participated in this comprehensive program, of which 1151 cases have sufficient information for inclusion in this study and others were excluded.

### Classification and diagnosis of diabetes

Diagnosis of diabetes in this study was accomplished by measuring fasting blood sugar (twice times FBS  $\geq$  126 mg/dl), based on the WHO criteria (13) or self-reported and based on a doctor's prescription. Then, the participants were divided into two groups of diabetics (n= 362) and non-diabetics (n= 789).

### Bone mineral density measurement

BMD was measured by dual-energy X-ray absorptiometry (DEXA) using Lexxos densitometry in left femoral neck and lumbar spine (L2 – L4) and the results were expressed based on T-Score. T-Score  $\leq$  -2.5 SD was considered as osteoporosis, -2.5  $<$  T-Score  $\leq$  -1 as osteopenia and T-Score  $>$  -1 was considered as normal (14). Smoking, hypothyroidism and hyperthyroidism, liver disease, kidney disease, cancer, fractures and the use of steroids were obtained from the self-report and interview.

### Statistical analyzes

Data were analyzed by SPSS 18 statistical software using t-test, chi-square and Pearson correlation statistical tests and  $P \leq 0.05$  was considered as statistically significant.

## Results

Among 1151 cases of elderly individuals who participated in this study, 362 cases were diabetic and 789 were non-diabetic patients. The average age of diabetic patients was  $68.9 \pm 6.93$  years and in non-diabetic group was  $68.68 \pm 7.09$  years ( $P=0.18$ ). The

Table 1. Demographic data and measured values of the elderly people in Amirkola

Variables		Mean $\pm$ SD	P-value
Age (years)	Diabetics	68.09 $\pm$ 6.93	0.18
	Non-diabetics	68.68 $\pm$ 7.09	
Spine BMD (g/cm <sup>2</sup> )	Diabetics	0.90 $\pm$ 0.19	0.001
	Non-diabetics	0.85 $\pm$ 0.18	
Spine Z score	Diabetics	-0.079 $\pm$ 1.37	0.001
	Non-diabetics	-0.59 $\pm$ 1.26	
Spine T score	Diabetics	-1.39 $\pm$ 1.55	0.001
	Non-diabetics	-1.77 $\pm$ 1.45	
Femur BMD (g/cm <sup>2</sup> )	Diabetics	0.85 $\pm$ 0.16	0.48
	Non-diabetics	0.84 $\pm$ 0.15	
Femur Z score	Diabetics	-0.44 $\pm$ 1.09	0.12
	Non-diabetics	-0.55 $\pm$ 0.99	
Femur T score	Diabetics	-1.38 $\pm$ 1.21	0.54
	Non-diabetics	-1.43 $\pm$ 1.13	
BMI (kg/m <sup>2</sup> )	Diabetics	28.10 $\pm$ 4.53	0.001
	Non-diabetics	26.93 $\pm$ 4.59	

mean spine BMD in the diabetic group was 0.90 $\pm$  0.19 g/cm<sup>2</sup> and in the non-diabetic group was 0.85 $\pm$  0.18 g/cm<sup>2</sup> (P= 0.001). The mean femur BMD in the diabetic group was 0.85 $\pm$  0.16 g/cm<sup>2</sup> and in the non-diabetic group was 0.84 $\pm$  0.15 g/cm<sup>2</sup>, the difference was not statistically significant (P= 0.48). Table 1 shows the demographic data and measured values of the two groups.

The prevalence of osteopenia and osteoporosis in diabetic patients was significantly lower than people without DM (Table 2). In this study, no significant differences were found between the two

groups according to smoking history, hypothyroidism and hyperthyroidism, liver disease, kidney disease, cancer, fractures and the use of steroids (Table 3).

As shown in Table 4, there were significant differences between the two groups for spine BMD in elderly men (P= 0.001). In addition, our results indicated that the femur bone mineral mass in diabetic men was higher than non-diabetics (P= 0.03).

Our findings also demonstrated that diabetic women in the elderly population of Amirkola had a

Table 2. Distribution and the percentage of bone mineral density in diabetics and non-diabetics patients among the elderly population of Amirkola

Variables		Diabetics N (%)	Non-diabetics N (%)	P-value
Spine BMD	Normal	143 (39.5)	221 (28)	0.001
	Osteopenia	135 (37.3)	313 (39.7)	
	Osteoporosis	84 (32.2)	255 (32.3)	
Femur BMD	Normal	138 (38.1)	264 (33.5)	0.28
	Osteopenia	159 (43.9)	379 (48)	
	Osteoporosis	65 (18)	146 (18.5)	

Table 3. Distribution and the percentage of variables affecting the bone density in diabetics and non-diabetics patients among the elderly population of Amirkola

Variables		Diabetics N (%)	Non-diabetics N (%)	P-value
Smoking history	Yes	62 (17.1)	154 (19.5)	0.33
	No	300 (82.9)	635 (80.5)	
Hyperthyroidism	Yes	4 (1.1)	7 (0.9)	0.72
	No	358 (98.9)	782 (99.1)	
Hypothyroidism	Yes	17 (4.7)	28 (3.5)	0.35
	No	345 (95.3)	761 (96.5)	
Liver disease	Yes	11 (3)	12 (1.5)	0.08
	No	351 (97)	777 (98.5)	
Kidney disease	Yes	2 (0.6)	4 (0.5)	0.92
	No	360 (99.4)	785 (99.5)	
Fractures	Yes	102 (28.2)	208 (26.4)	0.51
	No	260 (71.8)	581 (73.6)	
Cancer	Yes	1 (0.3)	7 (0.9)	0.24
	No	361 (99.7)	782 (99.1)	
The use of steroids	Yes	34 (9.4)	74 (9.4)	0.81
	No	319 (88.1)	690 (87.5)	
	Don't know	9 (2.5)	25 (3.2)	

higher spine BMD compared to non-diabetic women ( $P= 0.001$ ), whereas in femoral BMD no significant difference was observed between the two groups ( $P= 0.52$ ) (Table 5).

In elderly people with a BMI less than 25, lumbar spine BMD had a significant difference between diabetic and non-diabetic groups ( $P= 0.03$ ) whereas, this difference was not significant in the

Table 4. Quantitative variables associated with diabetes in the elderly men of Amirkola

Variables		Mean± SD	P-value
Age (years)	Diabetics	68.66± 7.38	0.43
	Non-diabetics	69.16± 7.20	
Spine BMD (g/cm <sup>2</sup> )	Diabetics	0.99± 0.18	0.001
	Non-diabetics	0.91± 0.17	
Spine Z score	Diabetics	0.19± 1.27	0.001
	Non-diabetics	-0.46± 1.20	
Spine T score	Diabetics	-0.62± 1.26	0.001
	Non-diabetics	-1.23± 1.22	
Femur BMD (g/cm <sup>2</sup> )	Diabetics	0.91± 0.15	0.03
	Non-diabetics	0.88± 0.15	
Femur Z score	Diabetics	-0.32± 0.98	0.001
	Non-diabetics	68.66± 7.38	
Femur T score	Diabetics	69.16± 7.20	0.43
	Non-diabetics	0.99± 0.18	
BMI (kg/m <sup>2</sup> )	Diabetics	0.91± 0.17	0.001
	Non-diabetics	0.19± 1.27	

(Number of diabetics= 175, Number of non-diabetics= 469)

Table 5. Quantitative variables associated with diabetes in the elderly women of Amirkola

Variables		Mean $\pm$ SD	P-value
Age (years)	Diabetics	67.555 $\pm$ 6.45	0.47
	Non-diabetics	67.99 $\pm$ 6.89	
Spine BMD (g/cm <sup>2</sup> )	Diabetics	0.81 $\pm$ 0.16	0.001
	Non-diabetics	0.76 $\pm$ 0.16	
Spine Z score	Diabetics	-0.33 $\pm$ 1.41	0.001
	Non-diabetics	-0.77 $\pm$ 1.33	
Spine T score	Diabetics	-2.11 $\pm$ 1.45	0.001
	Non-diabetics	-2.57 $\pm$ 1.41	
Femur BMD (g/cm <sup>2</sup> )	Diabetics	0.79 $\pm$ 0.14	0.52
	Non-diabetics	0.78 $\pm$ 0.13	
Femur Z score	Diabetics	-0.56 $\pm$ 1.17	0.97
	Non-diabetics	-0.56 $\pm$ 1.01	
Femur T score	Diabetics	-1.75 $\pm$ 1.25	0.56
	Non-diabetics	-1.82 $\pm$ 1.11	
BMI (kg/m <sup>2</sup> )	Diabetics	28.48 $\pm$ 4.97	0.26
	Non-diabetics	28.48 $\pm$ 4.82	

(Number of diabetics= 187, Number of non-diabetics= 320)

femoral BMD. These findings were also observed in patients with a BMI over 30, but there was no

differences between patients with a BMI greater than 25 and less than 30 between the two groups (Figure 1).

## Discussion

Diabetes is one of the most common chronic disorders worldwide and its many complications can severely affect quality of life. In addition, DM has many long term complications affecting almost all tissues. Bone involvement is one of the complications of DM. Several lines of evidence indicate that low bone mass at the hip, femoral neck and spine in both male and female patients with type 1 DM, may eventually lead to an increased risk of bone fracture. In contrast, in type 2 DM, investigations appear conflicting, and the exact mechanism of this is still unknown. The results of this study demonstrated that BMD of the lumbar spine was significantly greater in diabetics

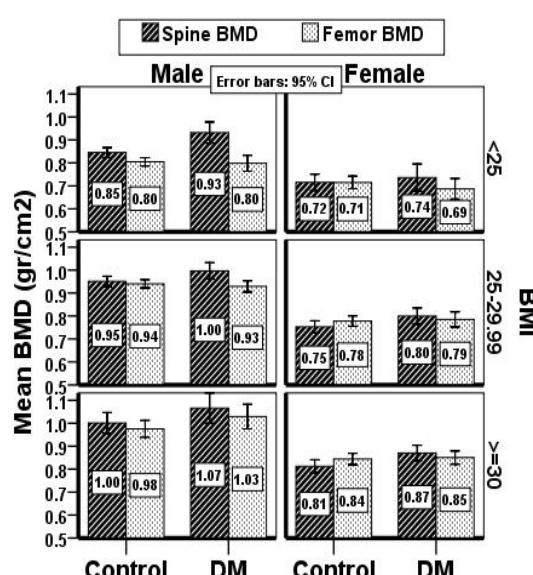


Figure 1. The relationship between lumbar spine and femoral neck bone mineral density and BMI according to gender in both diabetic and non-diabetic groups.

compared with non-diabetics patients, but no difference was observed for femur BMD between the two groups. In addition, the prevalence of osteopenia and osteoporosis was lower in diabetic patients compared with non-diabetics. Similar to our study, in a study conducted by Shan et al. on older Chinese women with type 2 diabetes, BMD at the lumbar spine was significantly higher than non-diabetic patients (15). Also, in Gupta's study in Kuwait performed on diabetic women, similar results were observed for lumbar spine BMD (16). In a study performed on women with type 2 diabetes by Hadzibegovic et al. in Croatia, the bone density of the lumbar spine and femoral neck in the diabetic group was significantly higher than the non-diabetic group (17). Similarly, Petit et al. reported a higher BMD in elderly patients with type 2 DM when compared to age-matched non-DM volunteers (18). In contrast, several other investigators reported a negative effect of type 2 DM on BMD and an increased fracture risk at several sites, including spine and hip has also been reported. For example, Bridges et al. observed no significant difference of BMD among diabetic patients (type 1 and 2) and the control group (19). In addition, Zhou et al. found that lumbar spine and femoral BMD in diabetic patients were significantly lower than the control group, which is not consistent with our study (20). The study of Anaforoglu et al. on elderly women with diabetes in Turkey showed that the prevalence of osteoporosis and osteopenia in patients with diabetes mellitus was not different from non-diabetic individuals (21). Nevertheless, these fractures and falls could have resulted from visual impairment from diabetic retinopathy, gait imbalance and overweight, all of which are common clinical features in type 2 DM. In addition, these conflicting results may be due to the different methods used to measure the bone density, the difference in duration of DM, severity and treatment

of diabetes. Moreover, insulin resistance and hyperinsulinemia can result in high rate of bone mineral mass in type 2 diabetic patients. Insulin is an anabolic hormone that increases bone mass through bone formation by insulin receptor substrate 1 (IRS-1) and IRS-2 on osteoblasts and by lowering sex hormone binding globulin (SHBG) concentration, which results in increased concentrations of estradiol and testosterone (22, 23). Our findings also revealed that the lumbar spine BMD in older women with diabetes were significantly higher than non-diabetic elderly women, but there was no significant difference between the two groups in femoral bone density. One similar study on diabetic and non-diabetic elderly women over 65 years in USA indicated that bone density in both spine and femur bone among women with diabetes was higher than non-diabetic women (24). Previous studies suggested that circulating androgen levels in men with type 2 diabetes was reduced, but was increased in women with type 2 diabetes. According to the above-mentioned mechanism, it is hypothesized that the conversion of androgens to estrogens in men may occur to a greater extent (25). Therefore, the bone density in both areas (lumbar spine and femoral neck) was significantly higher in diabetic male patients than non-diabetic patients (20). In addition, due to the cessation of ovarian function in older women during the menopausal period, there is a lack of estrogen. To justify these conflicting results, the genetic complexity of diabetes may be noted. Furthermore, many factors such as exposure to sunlight, vitamin D, number of pregnancies, exercise and dairy consumption can affect the prevalence of osteoporosis.

In conclusion, the results of the present study demonstrated that osteoporosis rate in diabetic patients was lower than in normal subjects, and BMD in elderly patients with diabetes was higher than non-diabetics. Although these results were

consistent with some previous studies, more investigations are required to clarify the possible cellular and molecular mechanisms.

### Conflict of interest

The authors declared no conflict of interest.

### Acknowledgement

The authors would like to thank the Deputy for Research at Babol University of Medical Sciences for financial support given to this project (Grant no.899917).

### References

1. Delaney MF, LeBoff MS. Metabolic bone disease. In: Ruddy S, Harris ED Jr, Sledge CD, eds. Kelley's Textbook of Rheumatology. 6th ed. Philadelphia: WB Saunders Co; 2001:1635-1652.
2. Holecki M, Wiecek A. Relationship between body fat mass and bone metabolism. *Pol Arch Med Wewn.* 2010;120:361-7.
3. Espallargues M, Sampietro-Colom L, Estrada M D, et al. Identifying bone-mass-related risk factors for fracture to guide bone densitometry measurements: a systematic review of the literature. *Osteoporos Int.* 2001;12:811-22.
4. Nicodemus K K, Folsom A R, Iowa Women's Health S. Type 1 and type 2 diabetes and incident hip fractures in postmenopausal women. *Diabetes Care.* 2001;24:1192-7.
5. Barrett-Connor E, Holbrook T L. Sex differences in osteoporosis in older adults with non-insulin-dependent diabetes mellitus. *JAMA.* 1992;268:3333-7.
6. van Daele P L, Stolk R P, Burger H, et al. Bone density in non-insulin-dependent diabetes mellitus. The Rotterdam Study. *Ann Intern Med.* 1995;122:409-14.
7. Lunt M, Masaryk P, Scheidt-Nave C, et al. The effects of lifestyle, dietary dairy intake and diabetes on bone density and vertebral deformity prevalence : the EVOS study. *Osteoporos Int.* 2001;12:688-98.
8. Tuominen J T, Impivaara O, Puukka P, et al. Bone mineral density in patients with type 1 and type 2 diabetes. *Diabetes Care.* 1999;22:1196-200.
9. Al-Maatouq M A, El-Desouki M I, Othman S A, et al. Prevalence of osteoporosis among postmenopausal females with diabetes mellitus. *Saudi Med J.* 2004;25:1423-7.
10. Strotmeyer E S, Cauley J A, Schwartz A V, et al. Diabetes is associated independently of body composition with BMD and bone volume in older white and black men and women: The Health, Aging, and Body Composition Study. *J Bone Miner Res.* 2004;19:1084-91.
11. Sahin G, Bagis S, Cimen O B, et al. Lumbar and femoral bone mineral density in type 2 Turkish diabetic patients. *Acta Medica (Hradec Kralove).* 2001;44:141-3.
12. Hosseini S R, Cumming R G, Kheirkhah F, et al. Cohort profile: the Amirkola Health and Ageing Project (AHAP). *Int J Epidemiol.* 2014;43:1393-400.
13. American Diabetes A. Standards of medical care in diabetes--2011. *Diabetes Care.* 2011;34 Suppl 1:S11-61.
14. National Osteoporosis Foundation. Clinician's Guide to Prevention and Treatment of Osteoporosis 2010. <http://www.nof.org/professionals/clinical-guidelines>. (Accessed 2012/9/10).
15. Cosman F, de Beur S J, LeBoff M S, et al. Clinician's Guide to Prevention and Treatment of Osteoporosis. *Osteoporosis Int.* 2014;25:2359-2381.
16. Shan P F, Wu X P, Zhang H, et al. Bone mineral density and its relationship with body mass index in postmenopausal women with type 2 diabetes mellitus in mainland China. *J Bone Miner Metab.* 2009;27:190-7.
17. Gupta R, Mohammed A M, Mojiminiyi O A, et al.

al. Bone mineral density in premenopausal Arab women with type 2 diabetes mellitus. *J Clin Densitom.* 2009;12:54-7.

18. Hadzibegovic I, Miskic B, Cosic V, et al. Increased bone mineral density in postmenopausal women with type 2 diabetes mellitus. *Ann Saudi Med.* 2008;28:102-4.

19. Petit M A, Paudel M L, Taylor B C, et al. Bone mass and strength in older men with type 2 diabetes: the Osteoporotic Fractures in Men Study. *J Bone Miner Res.* 2010;25:285-91.

20. Bridges M J, Moochhala S H, Barbour J, et al. Influence of diabetes on peripheral bone mineral density in men: a controlled study. *Acta Diabetol.* 2005;42:82-6.

21. Zhou Y, Li Y, Zhang D, et al. Prevalence and predictors of osteopenia and osteoporosis in postmenopausal Chinese women with type 2 diabetes. *Diabetes Res Clin Pract.* 2010;90:261-9.

22. Anaforoglu I, Nar-Demirer A, Bascil-Tutuncu N, et al. Prevalence of osteoporosis and factors affecting bone mineral density among postmenopausal Turkish women with type 2 diabetes. *J Diabetes Complications.* 2009;23:12-7.

23. Threlkill K M, Lumpkin C K, Jr., Bunn R C, et al. Is insulin an anabolic agent in bone? Dissecting the diabetic bone for clues. *Am J Physiol Endocrinol Metab.* 2005;289:E735-45.

24. Haffner S M, Bauer R L. Excess androgenicity only partially explains the relationship between obesity and bone density in premenopausal women. *Int J Obes Relat Metab Disord.* 1992;16:869-74.

25. Schwartz A V, Ewing S K, Porzig A M, et al. Diabetes and change in bone mineral density at the hip, calcaneus, spine, and radius in older women. *Front Endocrinol (Lausanne).* 2013;4:62.

26. Rasul S, Ilhan A, Wagner L, et al. Diabetic polyneuropathy relates to bone metabolism and markers of bone turnover in elderly patients with type 2 diabetes: greater effects in male patients. *Gend Med.* 2012;9:187-96.