https://doi.org/10.15218/zjms.2025.028

Prevalence and factors associated with osteoporosis in patients with type 2 diabetes mellitus

Received: 03/09/2023 Accepted: 22/10/2023

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Abstract

Background and objective: Diabetes mellitus is a long-lasting metabolic condition with significant morbidity and mortality. This study aimed to determine the prevalence of osteoporosis in type 2 diabetes mellitus patients using a Dual-energy x-ray absorptiometry (DEXA) scan and to find out the factors that are associated with osteoporosis.

Methods: A cross-sectional study was done on 100 type 2 diabetic patients attending the medical ward of Rizgary Teaching Hospital and outpatients of internal medicine and rheumatology in Erbil City from October 2017 to March 2018.

Results: Out of a hundred patients with type 2 Diabetes Mellitus, 28 were men and 72 were women. The prevalence of osteoporosis in type 2 diabetes mellitus was 40%. The age range was from 33-91 years (The mean age 59.5 years). Out of all collected patients, 44 were current smokers. In relation to anti-diabetic medications, among a total of 100 patients, only four of them relied on diet control alone. The majorities, 69 patients, were taking oral hypoglycemic drugs, six patients were exclusively on insulin therapy, whereas 21 diabetic patients were managing their condition through a combination of oral hypoglycemic drugs and insulin therapy. The minimum duration of Diabetes among patients was 2 years. The minimum range of serum vitamin D was six ng/ml while the maximum was 35 ng/ml (mean is 21.1). The minimum serum calcium was 7 mg/dl while the maximum number was 10.6 mg/dl (the mean is 9).

Conclusion: The prevalence of osteoporosis among diabetic patients was common. Significant association was found with old age, long duration of the disease, post-menopausal status of the female and low serum vitamin D level.

Keywords: Osteoporosis; Diabetes mellitus; Vitamin D; Calcium.

Introduction

Diabetes mellitus is a widespread disease in most parts of the world. The global diabetic population currently stands at 382 million individuals, and it is projected to escalate to 592 million by the year 2035.[1] Additionally, 316 million people with impaired glucose tolerance face a significant risk of developing the disease. This alarming figure is projected to reach 471 million by 2035. Moreover, the prevalence of type 2 diabetes is on the rise in all countries.[2] Diabetes mellitus is a long-lasting metabolic condition with significant morbidity and mortality, characterized by the presence of hyperglycemia.[3] Patients with diabetes mellitus have numerous skeletal disorders, including osteopenia or osteoporosis, Charcot's arthropathy, and diabetic foot syndrome.[4] Osteoporosis is characterized by a combination of diminished bone mass and modified bone quality, with microarchitectural abnormalities, resulting in decreased bone strength with an increased risk of fractures.[5] It was estimated that within the 27 countries of the European Union, approximately 22 million women and 5.5 million men have osteoporosis, resulting in a total of 3.5

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https://doi.org/10.15218/zjms.2025.028

million new fragility fractures. At present, the diagnosis of osteoporosis relies on a real bone mineral density (BMD) measurement using dual-energy x-ray absorptiometry (DEXA).[5] Osteoporosis is asymptomatic until there is a fracture. Despite experiencing a fracture, one out of every five women remains undiagnosed with osteoporosis.[6]

Osteoporosis is a condition that is frequently preventable. If left undetected, it can advance silently for numerous years without exhibiting symptoms until a fracture occurs.[5] Several factors increase the chance of developing osteoporosis. These include having a low body weight or a small frame, having a family history of the disease (especially for women), being postmenopausal, experiencing early menopause, having amenorrhea (lack of menstrual periods), using specific medications like glucocorticoids, insufficient calcium intake, lack of physical activity, smoking, and excessive alcohol consumption.[6]

The high occurrence of osteoporosis and diabetes mellitus is a cause for concern. In the United States, half of the elderly population suffers from osteoporosis, while diabetes or pre-diabetic conditions affect 20% of the overall population. Research unveiled that both diseases share common characteristics, encompassing molecular mechanisms and genetic predispositions.[7]

Serum osteocalcin concentration has been reported to be negatively associated with hemoglobin A1C (HbA1c) level. In patients with DM; osteocalcin, both in bone and serum is incompletely carboxylated, and the presence of undercarboxylated osteocalcin has been associated with adverse effects on energy metabolism and glucose regulation.[8]

Thiazolidinediones, such as rosiglitazone and pioglitazone, enhance insulin sensitivity by activating PPAR-γ. However, substantial clinical evidence suggests that these medications are associated with bone loss and an elevated risk of fractures.[9] Among the participants of the Studies of Osteoporotic Fractures, older diabetic women undergoing insulin treatment exhibited a risk of foot fractures that was more than double higher than that of non-diabetic individuals and non-insulin-using diabetic individuals. This observation suggests that insulin treatment may contribute to an increased fracture rate, likely due to the longer duration of the disease, a higher occurrence of diabetic complications, and more frequent episodes of hypoglycemia leading to frequent falls.[10]

This study aimed to determine the prevalence of osteoporosis in type 2 diabetes mellitus patients using a Dual-energy x-ray absorptiometry (DEXA) scan and to find out factors that are associated with osteoporosis.

Methods

Study design:
Cross-sectional, observational retrospective study.

Sample size: a total of 100 adult patients with type 2 Diabetes mellitus who had been admitted to the medical ward of Rizgary teaching hospital and outpatients of internal medicine and rheumatology were included.

Exclusion criteria, Endocrine disorder (Thyroid and parathyroid disease), renal disorder, hepatitis, those taken any known supplements or medications likely to affect bone metabolism such as calcium supplements, vitamin D, bisphosphonates, calcitonin, or hormones, chronic gastrointestinal disorder such as malabsorption and Crohn's disease.

Study Duration: Data collections were performed between October/2017 to March/2018.

Data collection: Diabetic patients were subjected to the standardized questionnaire on general risk factors for osteoporosis and risk of fractures. Required questions on the history of diabetes were included in the questionnaire for example (duration of diabetes, diabetes control by checking

https://doi.org/10.15218/zjms.2025.028

HbA1C, diabetes-specific therapy: diet, oral hypoglycemic agents including Sulfonylurea, Metformin, DPP4, TZD, and insulin). The questionnaire also included other risk factors for osteoporosis such as smoking habit (current, never, ex-smoker, and number of pack-year), alcohol consumption (current, never, and ex-drinker), calcium, and vitamin D deficiency.

According to menopausal status, all subjects were assigned to subgroups of postmenopausal (absence of menses in past 12 months) or premenopausal (regular menses in past 12 months). The weight and height of patients were measured and body mass index (BMI) was calculated using the formula [weight (kilogram) divided by square height (in meters)].[11]

Bone mineral density (BMD) was measured at the lumbar spine and femoral neck by dual-energy-ray absorptiometry (By using calculated T-scores, the patients were categorized into osteoporosis t-score <-2.5 SD, osteopenia t-score from -1 to -2.5 SD, and normal t-score >-1 SD.[7]

Data analysis:

The IBM Statistical Package for Social Science (SPSS), version 26, was used for data entry and analysis. A descriptive approach was used to determine frequencies and percentages, while for the analytic approach, Chi-square and t-test (unpaired t-test) were used to assess the association between categorical variables. A *P*-value of <0.05 was considered statistically significant.

Ethical consideration:

The study was approved by The Department of Medicine at the College of Medicine (HMU). All participants received a thorough explanation of the study's purpose, and their verbal consent was obtained after being fully informed. Participation in the study was voluntary, and respondents were guaranteed anonymity by not having to provide their names on the questionnaire, as well as that their answers would be kept private and confidential and used solely for research.

Results

In this study out of a hundred patients with type 2 Diabetes Mellitus 28 were men and 72 were women. Out of 72 women, 22 were premenopausal and 50 were post-menopausal. The age ranges from 33-91 years (The mean age was 59.5 Years). Out of all collected patients, 44 were current smokers, 55 were never smoked and 11 were ex-smokers. The minimum pack per year is 10 while the maximum is 30 packs per year (Mean is 19.9).

Regarding alcohol consumption from a total of 100 cases only 11 of them were current alcoholics and 89 of them never had Alcohol intake. In relation to anti-diabetic medications, among a total of 100 patients, only four of them relied on diet control alone. The majority, 69 patients, were taking oral hypoglycemic drugs. Six patients were. exclusively on insulin therapy, whereas 21 diabetic patients were managing their condition through a combination of oral hypoglycemic drugs and insulin therapy. (Table 1).

BMI ranged between 14.6-42.1 (mean BMI is 29.6). Regarding Diabetic control by checking HbA1C ranged between 6.5-14% (mean is 8.4). The minimum duration of Diabetes among patients was 2 years and the maximum was 33 years (mean is 10.5). serum vitamin D was checked as a risk factor forosteoporosis; the minimum range is 6 while the maximum is 35 (mean is 21.1). Also, serum calcium was checked the minimum number is 7 and the maximum number is 10.6 (the mean is 9) (Table 2).

Association between Osteoporosis and different measures:

In the present study, 100 patients with type 2 Diabetes Mellitus were evaluated with a DEXA scan. The overall prevalence of osteoporosis in this study was 40%, the prevalence of osteoporosis in men was 50.0% while in women was 36.1%. There was no significant association between gender and osteoporosis (*P*-value: 0.203). (Table 3).

https://doi.org/10.15218/zjms.2025.028

Table 1 Sociodemographic characteristics of the study sample

Variables	Values	Numbers	Percentages
Gender	Female	72	72
	Pre-menopausal	22	
	Post-menopausal	50	
	Male	28	28
Smoking	Current	34	34
	Ex-smoker	11	11
	Never	55	55
Diabetic medication	Diet	4	4
	OHD	69	69
	Insulin	6	6
	Mixed	21	21
Alcohol consumption	Current	11	11
	Never	89	89
Total		100	100

Table 2 Duration of Diabetes mellitus, Body mass index, HbA1C, Vitamin D and Calcium of the study sample

Measures	Range	Minimum	Maximum	Mean	S. D
BMI	27.4	14.6	42.1	29.6	5.5
HbA1C	7.5	6.5	14	8.4	1.6
Duration of Diabetes Mellitus	31	2	33	10.5	7.9
S. Vitamin D	29	6	35	21.1	8.8
S. Calcium	3.6	7	10.6	9	0.8

Table 3 Association between gender and osteoporosis

Gender	Osteoporosis			*P* value
	No No. (%)	Yes No. (%)	Total* No. (%)	
Male	14 (50)	14 (50)	28 (28)	
Female	46 (63.9)	26 (36.1)	72 (72)	0.203
Total	60 (60.0)	40 (40.0)	100 (100)	

*Column total was calculated.

https://doi.org/10.15218/zjms.2025.028

A statistically significant association was found between menopausal status and osteoporosis. Among premenopausal females, 18.2% were diagnosed with osteoporosis. On the other hand, among post-menopausal females, 44% had osteoporosis. Out of the total of 72 females included in the study, 26 (36.1%) were identified as having osteoporosis, while 46 (63.9%) did not have osteoporosis (*P*-value = 0.03). (Table 4)

The study showed that 47% of current smokers had osteoporosis, 30.9% of those who never smoked had osteoporosis and 63.6% of former smokers had osteoporosis. There was no significant correlation between smoking and osteoporosis (*P*-value = 0.07) (Table 5)

Table 4 Association between menopause and osteoporosis

Females	**Osteoporosis**		**Total***	
	No No. (%)	**Yes No. (%)**	**No. (%)**	***P* value**
Pre-menopause	18 (81)	4 (18.2)	22 (30.6)	
Post-menopause	28 (56)	22 (44)	50 (69.4)	0.03
Total	46 (63.9)	26 (36.1)	72 (100)	

*Column total was calculated.

Table 5 Association between smoking and osteoporosis

Smoking	**Osteoporosis**		**Total***	***P* Value**
	No No. (%)	**Yes No. (%)**	**No. (%)**	
Current	18 (52.9)	16 (47)	34 (34)	
Never	38 (69)	17 (30.9)	55 (55)	0.07
Former	4 (36.3)	7 (63.6)	11 (11)	
Total	60 (60)	40 (40)	100 (100)	

*Column total was calculated.

https://doi.org/10.15218/zjms.2025.028

Regarding the association between alcohol intake and osteoporosis, from a total of 11 patients with alcohol intake, 6 (54.5%) of them had osteoporosis, whereas in 89 nonalcoholic patients, 34 (38.2%) of them had osteoporosis and 55 (61.7%) didn't have osteoporosis. No significant association was detected between alcohol intake and osteoporosis (*P*-value = 0.29). (Table 6)

There was no significant association between anti-diabetic medications and osteoporosis. Interestingly, the highest prevalence of osteoporosis was found among patients using oral anti diabetic drugs (OHDs). Out of the total of 69 patients on OHDs, 31 (44.9%) were diagnosed with osteoporosis. Among the four patients relying on diet control alone, one (25%) had osteoporosis, out of the 21 patients receiving mixed therapy involving both OHDs and insulin, seven (33.3%) were diagnosed with osteoporosis. Notably, out of the six patients using insulin therapy exclusively, one (16.6%) had osteoporosis.

In summary, although different medication categories were observed, there was no significant association between the type of anti-diabetic medication and the prevalence of osteoporosis. Top of Form (*P* = 0.42). (Table 7)

Table 6 Association between alcohol and osteoporosis (*P* = 0.29)

Alcohol	Osteoporosis		Total*	
	No No. (%)	Yes No. (%)	No. (%)	*P* value
Current	5 (45.4)	6 (54.5)	11 (11)	
Never	55 (61.7)	34 (38.2)	89 (89)	0.29
Total	60 (100)	40 (100)	100 (100)	

*Column total was calculated.

Table 7 Association between anti-diabetic medications and osteoporosis

Medications	Osteoporosis		Total	
	No No. (%)	Yes No. (%)	No. (%)	*P* value
Diet	3 (75)	1 (25)	4 (4)	
Oral hypoglycemic drug	38 (55)	31 (44.9)	69 (69)	
Insulin	5 (83.3)	1 (16.6)	6 (6)	0.42
Mixed	14 (66.6)	7 (33.3)	21 (21)	
Total	60 (100)	40 (100)	100 (100)	

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A statistically significant difference was observed in the mean age between osteoporotic patients (65.35 years) and non-osteoporotic participants (55.67), with a *P*-value of 0.001. Furthermore, there is a significant association between the mean duration of diabetes and osteoporosis (14.45 years) compared to non-osteoporotic patients (8.00), with a *P*-value of 0.001. Additionally, a significant association was found between the mean serum vitamin D levels of osteoporotic patients (17.93) and non-osteoporotic patients (23.35), with a *P*-value of 0.002. (Table 8). There is no significant association between the mean of either pack per year, BMI, HbA1C, or serum calcium of osteoporotic, and non-osteoporotic patients as in all of them the *P*-value was more than 0.05. (Table 8).

Table 8 Association between the mean of different measures and osteoporosis

Parameters	Osteoporosis	N	Mean	S. D	*P*
Age (years)	Yes	40	65.35	12.46	0.001
	No	60	55.67	12.57	
Pack per year	Yes	23	21.30	5.04	0.15
	No	22	18.59	7.39	
BMI	Yes	40	29.14	6.48	0.45
	No	60	29.99	4.91	
Duration of Diabetes Millitus(years)	Yes	40	14.45	10.27	0.001
	No	60	8	4.27	
HbA1C	Yes	40	8.46	1.68	0.92
	No	60	8.43	1.55	
S. Vit D	Yes	40	17.93	8.92	0.002
	No	60	23.35	8.17	
S. Calcium	Yes	40	9.10	0.95	0.74
	No	60	9.05	0.69	

https://doi.org/10.15218/zjms.2025.028

Discussion

Diabetes Mellitus is a chronic metabolic disorder with substantial morbidity and mortality with many long-term complications affecting almost all tissues, bone involvement is one of the complications of DM.[5] In this observational retrospective study 100 patients with type 2 Diabetes Mellitus were evaluated with a DEXA scan for the presence of Osteoporosis and various risk factors were assessed. The overall prevalence of osteoporosis in this study was 40%; this is nearly similar to another study done in India in which the prevalence of osteoporosis in type 2 Diabetes was 35.5 %.[12]

In a study done in the Philippines, the prevalence-of osteoporosis among type 2 diabetes was 22.41%[13] This range is much lower than our study prevalence.

Our study did not find a significant link between gender distribution and osteoporosis (*P*-value = 0.20). However, in a Chinese study, gender proved to be a significant risk factor for osteoporosis in patients with T2DM. They observed that the prevalence of osteoporosis was much higher in female T2DM patients (44.8%) compared to males (37.0%).[14]

In this study there was a significant correlation between menopause females and osteoporosis, the prevalence of osteoporosis in premenopausal women was 18.2%, and in post-menopausal women was 44% (*P*-value = 0.03) as women lose bone more rapidly, particularly during the first 5–10 years after menopause due to estrogen deficiency.[15]

In our study, the age of patients ranged from 33 to 91 years and the mean was 59.5. There was a significant difference between mean age and osteoporotic patients (65.35) and non-osteoporotic participants (55.67). The *P*-value was 0.001. It is close to Xu H. et al study where the mean age among osteoporotic patients was 64.15 ± 7.75.[16]

In our study, there was a significant disparity in the mean duration of diabetes between patients with osteoporosis (14.45 years) and those without osteoporosis (8.00 years) with a *P*-value of 0.001. Similarly, in the study conducted by Nicodemus et al., it was observed that the duration of diabetes exceeding 13-40 years posed a significantly higher risk for hip fracture (RR 2.30, 95% CI 1.39-3.81).[17]

This study revealed a statistically significant association between serum vitamin D levels and osteoporosis, as most osteoporotic patients exhibited low serum vitamin D levels. Among the osteoporotic patients, the mean vitamin D level was 17.93, whereas, in non-osteoporotic patients, the mean was 23.35, with a *P*-value of 0.002.These findings align with the study conducted by Goldshtein et al., where vitamin D deficiency was notably more prevalent among osteoporotic patients with T2DM compared to osteoporotic patients without T2DM (29.2% vs. 21.6%).[18]

In our study, we did not find a statistically significant difference between BMI and osteoporosis in diabetic patients (*P*-value was 0.45). This contrasts with the findings of Xu H. et al., who observed that T2DM patients with osteoporosis and osteopenia had older age and lower BMI compared to T2DM patients with normal bone mineral density.[16]

Our study did not establish a significant correlation between diabetes control, as measured by HbA1C levels, and osteoporosis. The average HbA1C levels were 8.46 for osteoporotic patients and 8.43 for non-osteoporotic patients, with non-significant *P*-value of 0.92. This finding aligns with the study conducted by Vestergaard P., which also showed no association between HbA1C levels and osteoporosis.[19] However, it is worth noting that the study by Xu H. et al. detected a notable difference. They found that poor glycemic control (HbA1c > 7.5%) was associated with 63% increased odds of osteoporosis and osteopenia in male T2DM patients, but not in female T2DM patients with better glycemic control.[16]

Our study did not reveal any significant differences between osteoporosis and factors such as smoking, oral hypoglycemic drug use, and alcohol consumption. This finding is consistent with the results of Xu H. et al.'s study.[16] However, our findings are in contrast to the study by Nicodemus et al., which found that the use of insulin or oral diabetes medications in women with type 2 diabetes was associated with a higher rate of hip fractures.[17]

Conclusion

The prevalence of osteoporosis among diabetic patients was common. Significant association was found with age, duration of the disease, menopausal status of the female, serum vitamin D level while there was no significant association with gender, smoking, oral hypoglycemic drug, alcohol consumption, MI and HbA1C level.

Competing interests

The author declares that he has no competing interests.

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