Osteoporosis and Osteopenia Among Patients with Type 2 Diabetes Aged More Than 50 years and Role of Hypoglycemic Drug Therapy

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Abstract

Background: Both type 2 diabetes mellitus (T2DM) and osteoporosis affect a large proportion of older people around the world and are major public health threats. Though the relationship between T2DM and osteoporosis has been widely investigated, it remains controversial. However, the association between clinical characteristics (especially hypoglycemic drug use) and osteoporosis/osteopenia remains unclear. **Aim:** To decrease morbidities resulting from osteoporosis and osteopenia as a complication of type 2 diabetes among patients aged > 50 years. **Subjects and methods:** The study was a cross-sectional study, conducted in internal medicine department, faculty of medicine, ZagazigUniversity Hospital on 210 patients between January 2020 and January 2021. Complete history taking and full clinical examination and data gathering were done for all participants. HbA1c was measured using ion-exchange high performance liquid chromatography. Anti-diabetic medication use was obtained from medical records to assess their role. BMD at the lumbar spine (L1 - L4), the femoral neck, and total femoral was measured by dual-energy X-ray absorptiometry densitometer. **Results:** There is high statistically significant difference between normal and osteoporosis as regard L1-L4 T-score and significant difference as regard Femoral neck T-score. There was statistically significant association between glycemic control (HbA1C) and osteoporosis. As lower HbA1C (good glycemic control) was associated with normal patients without osteoporosis and higher HbA1C (bad glycemic control) was associated with osteoporosis patients among type 2 diabetes patients (p <0.001). **Conclusion:** A decreasing mean BMD trend had been observed in T2DM patients specially those aged more than fifty years.

KeyWords: Osteoporosis, Osteopenia, Diabetes, Hypoglycemic.

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Introduction

Diabetes mellitus (DM) is a chronic metabolic disorder with substantial morbidity and mortality, characterized by the presence of hyperglycemia. Pharmacotherapy, continuing medical care and education are crucial for preventing acute and chronic complications. On the other hand, osteoporosis (OP) is a painless weakening of the bones that constitutes an enormous socioeconomic crisis, with a harmful impact on morbidity and mortality. It leads to increased skeletal fragility and micro architectural deterioration of bone tissue, causing a decrease in bone mineral density (BMD), bone quality, and strength. Osteoporosis can result in height loss, severe back pain, deformity, impairments in a person's ability to walk, disability, and even death. [1]

Both type 2 diabetes mellitus (T2DM) and osteoporosis affect a large proportion of older people around the world and are major public health threats. T2DM could increase 1 to 3 time's risk of fractures according to recent evidence indicating that osteoporosis and other skeletal fragility-related disease should be considered as the complications associated with T2DM. [2]

Though the relationship between T2DM and osteoporosis has been widely investigated, it remains controversial. However, the association between clinical characteristics (especially hypoglycemic drug use) and osteoporosis/osteopenia remains unclear. Some studies showed that treatments with metformin, glucagon-like peptide-1 agonists, and the dipeptidyl peptidase-4 inhibitors had no effect on BMD or increased BMD, while thiazolidinedione's treatment, such as rosiglitazone and pioglitazone, was associated with the decreased BMD. [3].

Aim and objectives

To decrease morbidities resulting from osteoporosis and osteopenia as a complication of type 2 diabetes among patients aged > 50 years via exploring the associations of diabetic clinical characteristics and anti-diabetic treatments with osteoporosis and osteopenia in those patients.

Subjects and Methods

Technical design: The study was a cross-sectional study, conducted in internal medicine department, faculty of medicine, Zagazig university hospital on 210 patients between January 2020 and January 2021. We included type 2 diabetic patients elder than 50 years. In addition, we excluded patients having other systemic diseases affecting bone metabolism, using some medications affecting bone metabolism, such as estrogen or steroids, alcoholics, and cigarette smokers.

Methods: Complete history taking, and full clinical examination and data gathering were done for all participants. HbA1c was measured using ion-exchange high performance liquid chromatography. Anti-diabetic medication use was obtained from medical records to assess their role. BMD at the lumbar spine (L1 - L4), the femoral neck, and total femoral was measured by dual-energy X-ray absorptiometry densitometer.

Administrative considerations: Written informed consent was obtained from all participants after a clear explanation of the study. The study was approved by the ethical research committee of the Faculty of Medicine, Zagazig University (Institutional Research Board "IRB"). Furthermore, the work has been carried out under The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Statistical Analysis

Statistical analysis was performed using the Statistical Package for Social Science (SPSS Inc, Chicago) version 21 for Microsoft Windows. Descriptive statistics were used to examine the distribution of patients' characteristics and the outcomes. A single logistic regression model was applied to estimate the relationship between the risk factors as independent variables and eclampsia as the outcome. A P value < 0.05 was considered significant.

Results

According to outcome among our patients, 171 (81.4%) were normal and 39 (18.6%) were with Osteoporosis, as shown in Table (1). Relation between outcome and demographic data is demonstrated in Table (2). There is significant difference between normal and osteoporosis as regard gender and BMI. There is no significant difference between normal and osteoporosis as regard other demographic Data (Age). Table (3) clears the relation between outcome and examinations. There is no significant difference between diabetic with normal BMI and diabetic with osteoporosis as regard physical & laboratory

Examinations (Systolic, Diastolic and HbA1c). Relation between outcome and medication is cleared in Table (4). There is no significant difference between diabetic with normal or with osteoporosis as regard Anti-diabetic medication and Insulin treatment. Relation between outcome and BMD is analyzed in Table (5). This table shows that there is high statistically significant difference between normal and osteoporosis as regard L1-L4 T-score and significant difference as regard Femoral neck T-score. Relation between outcome and glycemic control (HbA1C) is demonstrated in Table (6). There was statistically significant association between glycemic control (HbA1C) and osteoporosis. As lower HbA1C (good glycemic control) was associated with normal patients without osteoporosis and higher HbA1C (bad glycemic control) was associated with osteoporosis patients among type 2 diabetes patients (p <0.001).

Table (1): Distribution of the studied cases according to outcome(n = 210).

Outcome	No.	%
Normal	170	81
Osteoporosis	40	19

Qualitative data is represented as number and percentage.

Table (2): Relation between outcome and demographic data (n = 210).

Demographic Data	Outcome				Test of sig.	p
	Normal (n=170)		Osteoporosis (n=40)			
	No.	%	No.	%		
Gender						
Male	70	41.2	24	60	X^2 = 4.640	**0.032***
Female	100	58.8	16	40		
Age (years)						
Min. – Max.	53 – 57		53 – 53.5		t= 0.588	0.557
Mean ± SD.	53.0 ± 0.32		53 ± 0.1			
BMI (kg/m²)						
Min. – Max.	23.0 – 31.50		24.10 – 29.0		t= 2.436*	**0.017***
Mean ± SD.	27.10 ± 2.35		26.39 ± 1.43			
Median	26.80		26.30			

X^2: Chi square test; t: Student t-test; p: p value for comparing between normal and osteoporosis; *: Statistically significant at p ≤ 0.05

Table (3): Relation between outcome and examinations (n = 210).

Examinations	Outcome		t	P
	Normal (n=170)	Osteoporosis (n=40)		
Systolic				
Min. – Max.	110.0 – 150.0	110.0 – 150.0	1.493	0.142
Mean ± SD.	128.83 ± 12.69	132.82 ± 15.55		
Median	130.0	140.0		
Diastolic				
Min. – Max.	65.0 – 80.0	65.0 – 80.0	0.684	0.495
Mean ± SD.	71.46 ± 5.96	72.18 ± 5.71		
Median	70.0	75.0		
HbA1c				
Min. – Max.	6.00-10.30	8.10-10.30	0.273	0.782
Mean ± SD.	8.03± 1.27	9.38± 0.58		
Median	7.95	9.40		

t: Student t-test; p: p value for comparing between normal and osteoporosis

Table (4): Relation between outcome and medication (n = 210).

Medication	Outcome				X^2	p
	Normal (n=170)		Osteoporosis (n=40)			
	No.	%	No.	%		
Anti-diabetic medication						
Sulfonylurea treatment	58	34.1	16	40.0	2.744	0.314
Metformin treatment	102	60.0	24	60.0		
Thiazolidinedione's treatment	10	5.9	0	0.0		
Insulin treatment						
no	84	49.4	24	60.0	1.453	0.228
yes	86	50.6	16	40.0		

X^2: Chi square test; p: p value for comparing between normal and osteoporosis

Table (5): Relation between outcome and BMD (n = 210).

BMD	Outcome		U	p
	Normal (n=170)	Osteoporosis (n=40)		
L1-L4 T-score				
Min. – Max.	–2.50 – 1.40	–3.50 —2.60	0.00*	<0.001*
Mean ± SD.	–0.41 ± 1.13	–3.05 ± 0.31		
Median	–0.40	–3.0		
Femoral neck T-score				
Min. – Max.	–0.90 – 1.80	–0.80 – 1.60	2360.0*	0.004*
Mean ± SD.	0.53 ± 0.82	0.11 ± 0.77		
Median	0.50	0.0		

U: Mann Whitney test; p: p value for comparing between normal and osteoporosis; *: Statistically significant at p ≤ 0.

Table (6): Relation between outcome and glycemic control (HbA1C).

Variable	Outcome		t	P
	Normal (n=170)	Osteoporosis (n=40)		
HbA1C				
Min. – Max.	6.00-10.30	8.10-10.30	6.530	**<0.001***
Mean ± SD.	8.03± 1.27	9.38± 0.58		
Median	7.95	9.40		

t; Student t test; p: p value for comparing between normal and osteoporosis; *: Statistically significant at p < 0.05

Discussion

Osteoporosis is a systemic skeletal disorder characterized by low bone mass, micro-architectural deterioration of bone tissue leading to bone fragility, and consequent increase in fracture risk. Hop ham and colleagues found that the underlying pathogenic mechanism of bone fragility in T2DM is complex and not fully understood. Not only decreased bone mass but also bone microstructure might contribute to bone fracture [4].

As well, Li and colleagues cleared that T2DM might affect bone quality and quantity, leading to a

change in the structural properties of bone mass. T2DM affects bone homeostasis, so related fractures are considered a result of T2DM. Several studies have already reported an increased fracture risk among T2DM patients. [5]

The aim of our study was to decrease morbidities resulting from osteoporosis and osteopenia as a complication of type 2 diabetes among patients aged > 50 years via exploring the associations of diabetic clinical characteristics and anti-diabetic treatments with osteoporosis and osteopenia in those patients.

According to outcome in our study, we found that 170 (81%) was normal and 40 (19%) was with osteoporosis. In contrast with us, Xu and colleagues conducted a similar study investigating the osteoporosis and osteopenia among patients with type 2 diabetes aged more than fifty years, a total of 1222 T2DM patients aged ≥ 50 were included in their study of all participants, the prevalence of osteoporosis and osteopenia were 9.2% and 41.3%, respectively, and they were higher in females than in males. After adjustment for potential confounders, the results showed that overweight and obesity were related to decreased odds of osteoporosis and osteopenia in both male and female T2DM patients, poor glycaemic control was associated with increased odds of osteoporosis and osteopenia in males, and metformin treatment was associated with decreased odds of osteoporosis and osteopenia in females. [6]

According to Yingke and Wu, the adjusted prevalence of osteoporosis among T2DM patients increased from 3.13% to 6.10%, and the linear trend was close to being statistically significant. For non-diabetic individuals, the adjusted prevalence of osteoporosis was stable during this period. The adjusted osteopenia prevalence of T2DM patients and non-diabetic people had a significant increase in the linear trend. [7]

Our findings revealed that there is significant difference between normal diabetic patients and osteoporosis as regard BMI. There is no significant difference between normal and osteoporosis as regard other demographic Data. Several studies revealed that the multiple linear regression results indicated that sex, age, race, previous fracture, BMI, smoking, and physical activity are significant for T2DM patients. Thus, these related risk factors might partially contribute to the declining trend in mean BMD. [8]

According to the results of Xu and colleagues, osteoporosis and osteopenia were higher in females than in males. After adjustment for potential confounders, the results showed that overweight were related to decreased odds of osteoporosis and osteopenia in both male and female T2DM patients. [6]

Among T2DM patients, men usually had a higher BMD mean than women. Despite of these results, Napoli and colleagues indicated that attention should be paid to men since their findings cleared that men with diabetes had a higher risk of fracture. [9]

Our results revealed that there is no significant difference between normal and osteoporosis as regard Examinations (Systolic, Diastolic and HbA1c).There is no significant difference between normal and osteoporosis as regard Anti-diabetic medication and Insulin treatment. Sundararaghavan and colleagues studied the Thiazolidinedione use and bone loss in older diabetic adults. They found during their work that antidiabetic medication of T2DM patients may play a role in the observed trend. [10]

Several studies investigated the effect of TZD on bone metabolism and found it is associated with increased adiposeness and impaired osteoblast genesis, which might lead to impaired bone formation and ultimately to fractures. Other studies found that two medications, eventide (a glucagonlike peptide 1 receptor agonist) and dapagliflozin (a sodium glucose cotransporter-2 inhibitor) increased the risk of bone fractures, while dipeptidyl peptidase-4 inhibitors were associated with decreased fracture risk. [11]

Poor glycaemic control was proved to be associated with increased odds of osteoporosis and osteopenia in males, and metformin treatment was associated with decreased odds of osteoporosis and osteopenia in females as regarding the findings of Xu and colleagues. [6]

According to bone mineral density among our patients (BMD), there is high statistically significant difference between normal and osteoporosis as regard L1-L4 T-score and significant difference as regard Femoral neck T-score. Sellmeyerand and colleagues did a study clearing that T2DM patients had a higher BMD than non-diabetic people. They also proved the high bone mineral density and fracture risk in type 2 diabetes as skeletal complications of inadequate glucose control. [12].

Conclusionand Recommendations

In conclusion, a decreasing mean BMD trend had been observed in T2DM patients specially those aged more than fifty years. The unfavorable trend indicates a future downward shift in the bone health of T2DM patients. We also concluded that better glycemic management and rational choice of antidiabetic medication might be promising to prevent osteoporosis in T2DM patients. We recommended the regular monitoring of bone health in diabetic patients specially those aged more than fifty years. Further longitudinal studies are warranted to explore the association between antidiabetic treatment and osteoporosis.

Author Contributions

Nema Abd El-Wanees Abd El-Shafy is the only author and has fully contributed to the manuscript.

Conflict of interest

Authors declare no conflict of interest.

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