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Associated Osteoporosis Factors In Patients With Type 2 Diabetes

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Abstract

Background: Fragility fractures are increasingly recognized as a complication of type 2 diabetes, with fracture risk that increases with disease duration and poor glycemic control. Yet the identification and management of fracture risk in these patients remains challenging. This review explores the clinical characteristics of bone fragility in adults with diabetes and highlights

Methods: A study of 101 type 2 diabetic patients aged 30 years and older was admitted to 175 Military Hospital for treatment from April 2018 to March 2019.

Results: Distribution of patients by sex was 45(44.6%) male with average age 65,16±10,57 and 56 (55.5%) female with average age 65,23±10,98. Total average age was 65,2±10,74 (p> 0,05). 36 (15 male and 21 female) patients had age < 60 years and 65 patients (30 male and 35 female) > than 60 years. We found strong correlation between height and weight vs bone density, middle correlation between BMI and bone density and weak correlation between age lumbar spine density. Strong correlation between disease duration and bone density. The correlation equals -0.52 for lumbar spine density and -0.572 for femoral neck density.

Conclusion: According to our research, main factors affecting bones in patients with T2DM are female sex, duration of T2DM more than 5 years, uncorrected glucose level and high BMI.

Keywords: osteoporosis, 2 type diabetes, density, fracture, bones, risk factors

1. Introduction

According to the latest data published in the IDF Diabetes Atlas 9th edition one in 11 adults globally have diabetes and 463 million adults are currently living with diabetes. It expected that 578 million people will have diabetes by 2030 and 700 million by 2045 [1]. Type 2 diabetes mellitus (T2DM) is a metabolic diseases characterized by hyperglycemia as a result of insulin secretion defects or insulin action insufficiency [2]. Diabetes mellitus is well known as the disease causing the largest number of complications (more than 100) [3]. Besides micro- or macrovascular complications, T2DM leads to various skeletal disorders, including osteoporosis and fractures [4].

Osteoporosis is a bone disorder with significant changes in bone structe, affecting millions of people around the world. Bone fragility is the worse outcome of the disease, which needs long term therapy and medical management, especially in the elderly [5]. At present, the diagnosis of osteoporosis rests on areal bone mineral density (BMD) measurement using dualenergy X-ray absorptiometry (DXA). The World Health Organization (WHO) defines osteoporosis as a BMD T-score of −2.5 or less. Furthermore, a concept has been realized that a potential relationship seems to exist between diabetes (mainly T2DM) and osteoporosis [6].

Only about 4% of the global osteoporotic fracture burden is statistically attributable to diabetes. Increasing prevalence of diabetes and the fact it may also be associated with greater risk for (injurious) falls, fragility fractures increasingly appear as a serious, yet neglected complication of this disease [7]. An increased fracture risk has also been reported in some studies of type 2 diabetes [8]. Type 2 diabetes (T2D) is associated with higher BMD which is supposed to be associated with lower risk of fracture in the general population [9]. Indeed, individuals with T2DM actually have higher risk of fracture, particularly hip fracture and vertebral fracture [10, 11]. In T2DM patients, bone mineral density (BMD) seems to be normal to elevated. Persons with T2DM might be at increased risk for bone fractures, despite having higher BMD. There are another factors affecting bone tissue, so bone fractures are not related to BMD.

The association of diabetes with fracture risk has differed depending on the location of fracture, sex, age, duration of diabetes, and the effect of diabetes medications. Longer disease duration, the presence of diabetic complications, inadequate glycemic control, insulin use, and increased risk for falls are all reported to increase fracture risk [12, 24, 25].

The main goal of our article is to study and evaluate factors influencing bone texture with further osteoporosis development in patient with T2DM.

2. Methods

A study of 101 type 2 diabetic patients aged 30 years and older was admitted to 175 Military Hospital for treatment from April 2018 to March 2019.

2.1. Standard selection

- Follow the standards of the American Council of American Diabetes Asociation 2014 diagnosis and classification of type 2 diabetes.
- Patients were measured bone density by the method of dualenergy X-ray absorption (DXA) on Hologic machine.
- Voluntary agreement to join the research.

2.2. Exclusion criteria

- The patient is in a condition of emergency, coma, acute disease.
- History or current use of drugs that affect bone density such as medications for osteoporosis, prolonged glucocorticoid, anti-epileptic drugs, thyroid hormone replacement drugs etc.
- Patients suffering from conditions related to bone metabolism such as trauma, rheumatoid arthritis, multiple myeloma, Cushing's syndrome, hyperparathyroidism, chronic kidney and liver diseases such as cirrhosis, kidney failure.
- Patients on corticosteroid doses of ≥ 7.5mg per month.
- Patients with predisposing factors for osteoporosis: Early menopause before age 40, ovarianectomy, abdominal liposuction surgery.
- Patients do not agree to participate or not cooperate in the research process.

Our research present a horizontal cut representation.

2.3. Sample size and sample selection (1)

$$N = \frac{Z^2_{(1-\alpha/2)} p(1-p)}{d^2}$$

(1)

where p is the rate of osteoporosis in type 2 diabetic patients, this rate is 37.7%

so choose p = 0.377.

Thus the minimum sample size is: 91.

Our study provides 101 randomly selected patients.

All the procedures used in the work were following the ethical standards of the responsible committee on human experiments and the 1975 Helsinki Declaration, revised in 2000. All patients agreed to participate in the experiment and did not deny the results of the experiment, which will be presented in the given research paper.

3. Results and Discussion

3.1. Antropomethry

Distribution of patients by sex was 45(44.6%) male with average age 65,16±10,57 and 56 (55.5%) female with average age 65,23±10,98. Total average age was 65,2±10,74 (p> 0,05). 36 (15 male and 21 female) patients had age < 60 years and 65 patients (30 male and 35 female) > than 60 years. Mean height of both male and female group was 157.99±7.71 cm, mean weight 57.98±9.92 kg, mean body mass index (BMI) 23,23±3,58 kg/cm2. Structure of BMI was following: 52.48% of patients had BMI > 23, 38.61% of patients had BMI value 18-23 and 8.91% of patients had BMI < 18. Middle value of waist circumference was 71,04±10,09 and middle value of buttock circumference was 89,85±7,87. Most of patients shoved elevated blood sugar level and HbA_1c (Table 1).

3.2. Characteristics of bone density, osteoporosis rate and predicted fracture risk according to FRAX model

Average density among patients for different bones was following: 0,66±0,13 g/cm2 for femoral neck, 0,85±0,16 g/cm2 for whole femoral neck and 0,87±0,17 g/cm2 for lumbar spine. Among all patients, 43 (42.6%) had normal T-score of lumbar spine, 40 (39.6%) had decreased bone density and 18 (17.8%) had osteoporosis of lumbar spine. Simultaneously 38 (37.6%) had no pathology of femoral neck, 45 (44.6%) had decreased bone density and 18 (17.8%) had osteoporosis of femoral neck. Stratification of bone fracture risk by FRAX was following: 11 patients had high risk of bone fracture not basing on the bone density and 14 patients had high risk of fracture basing on bone density. Average bone fracture probability for the next 10 years in type 2 diabetics with osteoporosis was significantly higher in patients with osteoporosis 2,96±1,66 vs 0,75±0,74 in patients without osteoporosis ($p < 0.05$). We found strong correlation between height and weight vs bone density, middle correlation between BMI and bone density and weak correlation between age lumbar spine density (Table 2).

Conventional clinical risk factors can be employed to identify patients with diabetes at increased fracture risk, although risk assessment tools like FRAX do not fully capture these increased risks and thus systematically underestimate the risk of osteoporosis-related fractures in patients with type 2 diabetes [23].

Prevalence of osteoporosis by risk factors for decreased bone density was following:

- By age: 6 (5.9%) patients < 60 years old and 21 (20.8%) patients ≥ 60 years old
- By sex: 4 (4%) male and 23 (22.8%) female.
- By BMI: 15 (14.9%) patients ≤ 23 and 12 (11.9) > 23.

Patients with diabetes have greater BMD but poor bone microarchitecture associated with reduced bone strength [16]. It might be expected that obesity, which is a strong risk factor for type 2 diabetes, would protect against osteoporosis because of the known positive correlation between body mass index (BMI) and BMD. Indeed, type 2 diabetes is usually associated with a 5 to 10% higher areal BMD than healthy subjects, though there is significant heterogeneity between studies [17]. Nevertheless, data have clearly confirmed that while BMD systematically underestimates fracture risk, it still stratifies fracture risk in elderly patients with diabetes [21].

We found that weakest bone density was observing in patients with longest disease duration (more than 10), also femoral neck density was significantly lower comparing with lumbar spine density (Table 3).

A biphasic pattern has been proposed where fracture risk is in fact decreased in newly diagnosed type 2 diabetes, −which could be related to some protective effects of increased fat mass in these subjects–, and only increases significantly after 5 years [14]. In FRAX-adjusted analyses, only duration longer than 10 years was associated with a higher risk [15].

We found a strong correlation between disease duration and bone density. The correlation equals -0.52 for lumbar spine density and -0.572 for femoral neck density. Fasting blood sugar level and HbA1c level had no significant correlation with bone density. Most of patients showed osteoporosis also had elevated blood sugar level, HbA_1c, disease duration more than 5 years (Table 4).

Also we found medium and high correlation between patient's height and bone density: 0,349 for lumbar spine and 0.502 for femoral neck and weight and bone density: 0,547 for lumbar spine and 0,475 for femoral neck. Strong factors of osteoporosis development in patients with T2DM were: overweight or obesity and disease duration more than 5 years. Female also were more predictable to have osteoporosis (Table 5 and Table 6).

Leslie et al. recently published that in a large registry-based study for Manitoba, women with diabetes had marginally greater BMD loss at the femoral neck but not at other sites compared to a control population without diabetes [18]. Osteoporosis and type 2 diabetes mellitus are commonly observed in the elderly population and will likely increase in the future [22]. Findings of increased BMD and body weight, coupled with older epidemiological studies suggesting no increase or even a decrease in fracture risk led to speculation that patients with type 2 diabetes could have a decreased risk of osteoporosis. However, recent epidemiological and clinical studies provide substantial evidence for an increased fracture risk in patients with type 2 diabetes, despite an increased BMD or independently of BMD.

Certain individuals with diabetes seem to be at greater risk of fracture than others. Hence, in type 2 diabetes, age and duration of diabetes are clearly important [13]. Tight glycemic control (HbA1c 6.5–

6.9%) was associated with the lowest risk of fracture in a large cohort of elderly patients with diabetes. However, both hypoglycemia and hyperglycemia are associated with increased risk of fractures and falls, though probably via different mechanisms [19]. Recent observational and association studies reported increased fracture risk with worsening control as defined by glycated hemoglobin A1c (HbA1c) levels ≥ 7% [20].

During our research we found that combination of medication and insulin injection showed lowering of bones fracture comparing with sole treatment (Table 7).

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4. Conclusions

The incidence of fractures increased with age and was higher in T2DM w than in T2DM women. Overweight or obesity and disease duration more than 5 years also showed an important role in osteoporosis development. Uncorrected glucose level is one of the major factors for osteoporosis development. Females or older adults with T2DM required early clinical prevention as they were more vulnerable to osteoporosis. Also strong correlation between height and weight vs bone density was founded. We found that combination of medication and insulin injection showed lowering of bones fracture comparing with sole treatment. Although the relationship between diabetes and osteoporosis has been widely investigated, it remains controversial.

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Table 1. Some clinical features, subclinical diabetes

Characteristics		N	Ratio (%)
Duration of diabetes (year)	< 5	23	22,8
	5-10	46	45.5
	> 10	32	31.7
Fasting blood sugar level	< 7.0 mmol/l	21	20.8
	≥ 7.0 mmol/l	80	79.2
HbA_1c	≤ 6.5%	30	29.8
	> 6.5%	71	70.2
The means of HbA_1c ($\overline{X}$ ± SD) (%)		8.59±2.77	

Table 2. Correlation between age, height, weight, BMI and bone density

Index		lumbar spine density	femoral neck density
Age	r	-0.034	-0.282

	p	>0.05	<0.05
Height	r	0.349	0.502
	p	<0.05	<0.05
Weight	r	0.547	0.475
	p	<0.05	<0.05
BMI	r	0.364	0.194
	p	<0.05	>0.05

Table 3. Average bone density in patients with some clinical, subclinical characteristics of diabetes

Characteristics		lumbar spine density(g/cm^2) ($\overline{X}$ ± SD)	femoral neck density(g/cm^2) ($\overline{X}$ ± SD)
Fasting blood sugar level (mmol/l)	> 7	0.87±0.18	0.67±0.14
	≤ 7	0.89±0.17	0.62±0.12
	p	>0.05	>0.05
HbA_1c (%)	> 6.5	0.85±0.17	0.67±0.14
	≤ 6.5	0.91±0.19	0.66±0.14
	p	>0.05	>0.05
disease duration (years)	< 5	1.04±0.17	0.79±0.14
	5 - 10	0.85±0.15	0.65±0.11
	> 10	0.79±0.13	0.59±0.1
	p	<0.05	<0.05
Treatment regimen	Medicine	0.86±0.14	0.64±0.13
	Insulin injection	0.87±0.18	0.67±0.14
	Combined	1.06±0.22	0.72±0.08
	p	>0.05	>0.05

Table 4. Relationship between some characteristics of type 2 diabetes and the rate of osteoporosis

Characteristics		Osteoporosis (n,%)		p
		yes	no	
blood sugar level	< 7.0 mmol/l	8 (7.9)	13 (12.9)	>0.05
	≥ 7.0 mmol/l	19 (18.8)	63 (60.4)	

HbA_1c	≤ 6.5 %	6 (6.7)	19 (21.1)	>0.05
	> 6.5 %	17 (18.9)	48 (53.3)	
disease duration	< 5 years	1 (1)	22 (21.8)	<0.05
	≥ 5 years	26 (25.7)	52 (51.5)	
treatment regimen	medicine	9 (8.9)	21 (20.8)	>0.05
	Insulin injection	18 (17.8)	50 (49.5)	
	Combined	0 (0)	3 (3)	

Table 5. Multivariate linear regression analysis of factors related to bone density reduction.

Variable	β	OR	p
Age > 60	0.718	2.05	>0.05
Sex (female)	2.102	8.179	<0.05
Overweight and obesity	-2.046	0.129	<0.05
disease duration ≥ 5 years	2.697	14.832	<0.05
Fasting blood sugar level > 7mmol/l	0.735	2.085	>0.05
HbA_1c > 6.5%	-0.018	0.982	>0.05

Table 6. Multivariate regression analysis of factors related to osteoporosis

Variable	β	OR	p
Age > 60	1.422	4.147	<0.05
Sex (female)	2.355	10.326	<0.05
Overweight and obesity	-0.868	0.42	>0.05
disease duration ≥ 5 years	20.529	1.275	>0.05
Fasting blood sugar level > 7mmol/l	-0.167	0.846	>0.05
HbA_1c > 6.5%	-0.167	0.846	>0.05

Table 7. The average probability of bone fractures in the next 10 years.

treatment regimen	Mean ($\overline{X}$ ±SD) %	
	femoral neck fracture	general bone fracture
Only medication (n=30)	1.69±1.59	4.19±2.47
Insulin injection only (n=68)	1.22±1.38	3.49±2.26
medication and inject insulin (n=3)	0.53±0.05	2.03±0.45

P	>0.05	>0.05