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Research Paper

Bone Mineral Density in a Sample of Patients with Type 1 and Type 2 Diabetes Mellitus

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ABSTRACT:

BACKGROUND:

Diabetes, whether type 1 or 2, is one of the world's biggest health problems. The disease may affect all organ systems. The relationship between diabetes and bone mineral density (BMD) is a matter of debate.

OBJECTIVE:

To assess the effect of type 1 diabetes mellitus (T1DM) and type 2 diabetes mellitus (T2DM) on the bone mineral density in adult patients.

PATIENTS AND METHODS:

This is a cross-sectional study which included a total of 25 patients with T1DM, 25 patients withT2DM and other 25 apparently healthy subjects. Bone mineral density was measured using densitometry. Serum calcium, phosphorus, alkaline phosphatase (ALP were measured spectrophotometrically.

RESULTS:

Hip BMD and spine BMD were higher in T2DM (1.24±0.19 g/m^2, and 1.22±0.22 g/m^2, respectively) than T1DM (0.94±0.78 g/m^2 and 11.02±0.3 g/m^2, respectively) with significant difference. In T1DM group, spine Z-score had a positive significant correlation with BMI (r= 0.882, p<0.001). In T2DM group, Spine Z-score also had significant positive correlation with each of weight (r= 0.913, p<0.001) and BMI (r= 0.952, p<0.001).

CONCLUSION:

Patients with T1DM have lower BMD in terms of spine and hip Z-score than patients with T2DM or healthy controls. Bone mineral density parameters positively correlate with body weight and BMI.

KEYWORDS: Diabetes mellitus, mineral density, serum calcium and phosphorus.

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INTRODUCTION:

Individuals with poorly controlled diabetes are more likely to develop diabetic complications such as macrovascular disease, retinopathy, nephropathy, and neuropathy. Another notable diabetes consequence that has recently been identified is an increased risk of fragility fractures [1]. Two meta-analyses found that people with diabetes have an increased risk of hip fractures, and this is more prominent in type 1 diabetes, though type 2 diabetes patients had a 1.34 relative risk compared to nondiabetic populations. Surprisingly, the link between diabetes and bone fracture risk exists in both men and women [2,3].

Many research conducted around the world looked into the link between diabetes and bone fracture. The Nurses' Health Study tracked the occurrence of hip fractures in 109,983 women aged 34 to 59 for over 20 years. They discovered that the probability of hip fracture in women with T1DM was six times higher than in women without diabetes [4].

The Women's Health Initiative observational cohort monitored 93,676 typically healthy postmenopausal women over 7 years. After controlling for several factors, including frequency of falls, women with T2DM had a 20% higher risk of fracture at any site [5].

In a healthy human, bone is a dynamic tissue that undergoes continual remodeling to preserve the skeleton's biomechanical competency, prevent lesions, and contribute to mineral homeostasis. Each year, around 25% of trabecular bone and 3% of cortical bone are renewed in a process governed by mechanical, hormonal, and local variables.

If this remodeling process is disrupted, the result is normal or high density bone with an increased risk of fracture [6].

Hyperglycemia was found to be a risk factor that associated with decreased osteoclast function, motility and maturity. These facts are based on a study that used cell models measuring the effect of exposure to a high glucose concentration on osteoclastogenesis induced by receptor activator of nuclear factor kappa beta (NF-κB) [7].

Hyperinsulinism which precedes T2DM has been hypothesized as one of the critical factors for understanding the diabetic paradox [8]. In contrast to the density loss that occurs in T1DM, which begins with insulinopenia in the early stages of life and prevents the accomplishment of acceptable peak bone mass, insulin may be implicated in the rise of bone mineral density in T2DM patients. In a recent review, Meier et al. [9] highlighted the significance of using specific anti-diabetic medications for bone safety. Glitazones and type 2 sodium-glucose cotransporter (SGLT-2) inhibitors should be specifically mentioned in this context due to the potential rise in fracture risk [10, 11].

BMD can be assessed in a variety of ways and at different bone locations. The gold standard for noninvasive BMD measurement is still central dual-energy x-ray absorptiometry DXA, which measures BMD in grams/centimeter2 (g/cm2). In order to calculate BMD, Central DXA measures the area of the bone as well as the bone's bone mineral content (BMC) [12]

$$\mathrm{BMD}(\mathrm{g/cm^2}) = \frac{\mathrm{BMC\ in\ grams(g)}}{\mathrm{Area\ in\ centimeters(cm^2)}}$$

PATIENTS AND METHODS:

This is a cross-sectional study which included a total of 25 patients with T1DM, 25 patients with T2DM and other 25 apparently healthy subjects who were attending Al-Imamain Al-Kadhumain Medical City/ Baghdad during the period from January 2020 to December 2020.

Inclusion Criteria

- Adult patients with T1DM and T2DM of both sexes

Exclusion Criteria

- Malabsorption syndromes
- Malignant diseases
- Vitamin D deficiency
- Celiac disease
- Chronic pancreatitis or pancreatectomy
- Thyroid function abnormalities,
- Inflammatory disorders such as rheumatoid arthritis, systemic lupus erythematosus, Postmenopausal women or those with history of hysterectomy
- Patients under steroid therapy, immunosuppressants, anticonvulsants and calcium and Vitamin D supplements.

RESULT:

Clinical Characteristics of the Study Population Spine T-score was significantly higher in controls (0.58±1.12) than T1DM group (-0.41±1.12) with a significant difference, and T2DM group (0.16±1.713) with no significant difference. Likewise, both hip BMD and spine BMD were higher in T2DM (1.24±0.19 g/m^2, and 1.22±0.22 g/m^2, respectively) than T1DM (0.94±0.78 g/m^2 and 11.02±0.3 g/m^2, respectively) with significant difference, Otherwise, each of spine Z-score, hip T-score and hip Z-score demonstrated comparable values in different groups with no significant differences. The incidence of osteopenia and osteoporosis were comparable between in T1DM (36% and 4%, respectively), T2DM (40% and 4%, respectively) and controls (16% and 0%, respectively) with no significant differences (Table 1).

Table 1: Clinical characteristics of the study population.

Variables	T1DM (n=25)	T2DM (n=25	Controls (n=25)	P1		P2	P3
Spine T-score Mean±SD Range	-0.41±1.12 -2.6- 1.7	0.16±1.713 -2.7-3.6	0.58±1.12 -1.4-2.3	0.468		0.019	0.569
Spine Z-score Mean±SD Range	0.08±1.21 -2.0-1.9	0.66±1.59 -2.0-3.8	0.9±0.82 -0.9-2.4	0.107		0.069	0.497
Hip T-score Mean±SD Range	0.23±1.0 -1.3-2.3	0.63±1.5 -1.4-3.6	0.7±0.9 -1.5-2.0	0.230		0.155	0.820
Hip Z-score Mean±SD Range	0.53±0.9 1.2-2.5	1.02±1.38 -1.3-3.8	0.89±0.66 -0.9-2.4	0.094		0.216	0.656
Hip BMD, g/cm^2 Mean±SD Range	0.94±0.78 0.7-1.4	1.24±0.19 0.97-2.0	1.11±0.13 0.89-1.3	0.02		0.199	0.068
Spine BMD, g/m^2 Mean±SD Range	1.02±0.3 0.1-2.0	1.22±0.22 0.89-1.92	1.09±0.13 0.89-1.3	0.01		0.968	0.089
Osteopenia No Yes	16(64%) 9(36%)	15(60%) 10(40%)	21(84%) 4(16%)	0.771		0.107	0.059
Osteoporosis No Yes	24(96%) 1(4%)	24(96%) 1(4%)	25(96%) 0(0%)	1.0		0.312	0.312

P1: between T1DM and T2DM, P2: between T1DM and controls, P3: between T2DM and controls

Association of BMD Parameters with the Categorical Variables

In T1DM, the median spine T-score in patients with osteopenia was -2.0 compared with -0.45 in patients without osteopenia with a significant difference. Similarly, the median value of spine T-score, spine Z-score and hip T-score in patients with osteoporosis was -2.6, -2.0 and -1.3, respectively compared with -0.3, 0.05 and 0.15, respectively in patients without osteoporosis with significant differences (Table 2).

In T2DM, the median value of spine T-score, spine Z-score, and hip Z-score hip T-score in patients with osteoporosis was -1.15, -0.95, -0.9 and -0.85, respectively compared with 1.8, 1.7, 1.6 and 1.7, respectively in patients without osteoporosis with significant differences. On the other hand, median value of spine T-score in patients with osteoporosis was -2.7, respective compared with 0.1 in patients without osteoporosis with a significant difference (Table 2).

In controls, patients with IHD had significantly lower spine T-score than those without IHD (-1,25 versus 1.1). Furthermore, patients with other comorbidities demonstrated lower spine T-score and spine Z-score (-1.25 and -0.9, respectively) than those without such comorbidities (1.1 and 1.2, respectively). Finally, the median value of spine T-score and spine Z-score in patients with osteoporosis was -1.162 and -0.1, respectively compared with 1.1 and 1.2, respectively in patients without osteoporosis with significant differences (Table 2).

Table 2: Association of BMD parameters with the categorical variables in T1DM patients.

Variables	Spine T-score	Spine Z-score	Hip T-score	Hip Z-score	Spine BMD	Hip BMD
Gender						
Male	-0.75	0.1	0.05	0.7	1.0	1.05
Female	-0.3	-0.2	0.1	0.3	1.13	1.00
p-value	0.728	0.936	0.810	0.611	0.503	0.728
Smoking						
Never	-0.6	0.1	0.05	0.7	1.0	1.05
Ex/current	-0.15	-0.2	0.1	0.3	1.13	1.0
p-value	0.198	0.877	1.00	0.514	0.598	0.333
Osteopenia						
No	-0.45	0.15	0.15	0.3	0.3	1.0
Yes	-2.0	-0.05	1.2	1.13	1.2	1.2
p-value	0.001	0.187	0.677	0.329	0.452	0.846
Osteoporosis						
No	-0.3	0.05	0.15	0.7	1.08	1.0
Yes	-2.6	-2.0	-1.3	-0.9	1.0	0.8
p-value	0.04	0.042	0.048	0.214	0.712	0.320

Data were expressed as medians and Mann Whitney test was used for comparison

DISCUSSION:

This study aimed to assess the effect of T1DM and T2DM on the BMD in adult men and women.

According to the results of this study, spine T-score and spine BMD were significantly higher in T2DM than T1DM, while there were no significant differences between T2DM and controls. In accordance with these results are many studies worldwide. In a meta-analysis including 46 studies with a total of 2,617 case and 3,851 control subjects, Loxton et al. [2021] found that patients with T1DM had lower BMD in lumbar spine, femur, tibial trabecular, radial trabecular, phalangeal and calcaneal regions compared with age-matched healthy controls. In an American study Mastrandrea et al. [14] showed that BMD remained to be lower in patients with T1DM compared with control subjects at the total hip, femoral neck, and whole body even after adjusting for age, BMI, and oral contraceptive use. Asokan et al. [15] conducted a cross-sectional study on 75 T2DM patients and 75 nondiabetic subjects. BMD was measured and the results were paralleled with age-matched subjects. Both T1DM and T2DM showed comparable BMD with no significant difference.

Tuominen et al. [16] assessed BMD in 56 T1DM and 68 T2DM patients and 498 nondiabetic community control subjects. BMD values were significantly lower in T1DM patients than T2DM patients or the control subjects. Almost similar results to the present were obtained by two other studies that reported no significant difference in BMD values between T2DM and control subjects [17,18].

Vestergaard [19] and revealed that BMD was lower at hip and spine in T1DM, while Strotmeyer [20] revealed that older age and longer duration of T1DM were associated with lower BMD.

On the other hand, several reported demonstrated contradictory findings. Bilha et al. [21] showed that T2DM patients had equivalent BMD compared to T1D individuals (after controlling for age, BMI, and illness duration) and to matched controls, respectively. Sauque-Reyna et al. [22] showed that T2DM patients had significantly higher BMD than controls in a Spanish research that included 245 patients with T2DM and 205 healthy controls.

These discrepancies may be explained by methodological differences and diverse patient selection criteria. For example, in the Rotterdam study [23], which showed higher than normal BMD in T2DM patients, many of the patients had newly undiagnosed diabetes, whereas in our patients, T2DM was of long duration and required insulin therapy.

Despite this contradiction, there is almost general agreement about the low BMD in T1DM patients. Several mechanisms have been suggested to clarify this drop in BMD.

T1DM is associated with devastation in pancreatic β cells which results in insulin deficiency and hyperglycemia. Hyperglycemia influences the development of bone in different domains: it harms osteoblast either directly or through

its role in suppressing gene expression that responsible for the maturation of osteoblast [24], it increases PPARγ that promote adipogenesis from mesenchymal stem cells at the expense of bone formation thus decreasing the bone accrual and peak bone mass [25]. Furthermore, Glitazones, insulin drugs, are agonists of PPARγ and they are linked to more fractures and low bone mass [26], hyperglycemia also induces the expression of proinflammatory cytokines like TNFα which inhibits osteoblast differentiation and activity, thus increasing osteoblastic apoptosis [27]. In addition, hyperglycemia may result in the generation of increase reactive oxygen species (ROS) which in turn can increase osteoclast formation and activity [28].

In contrast, the normal or even above normal level of BMD in T2DM in some studies has been explained Based on the metabolic alterations observed in patients with DM, such as hyperinsulinemia, elevated levels of IGF-1, hyperandogenism and hyperleptinemia. It is known that insulin has an anabolic and beneficial role on osteogenesis through interaction with the IFG-1 receptor abundant in osteoblasts, 57.58 in addition to maximizing the effect of PTH on osteoblasts [29]. Furthermore, it must be considered that a higher proportion of T2DM patients ingested calcium and vitamin D, drugs that they can favorably modify BMD [22].

CONCLUSION:

1. Patients with T1DM have lower BMD in terms of spine and hip Z-score than patients with T2DM or healthy controls
2. Type 2 DM is not associated with reduction nor with increase in BMD parameters.
3. Bone mineral density parameters positively correlate with body weight and BMI, and negatively correlated with ALP in patients with T1DM and T2DM.

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