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Osteocalcin,Bone Mineral Density,Vitamin D, And Homa-Ir Inpostmenopausaliraqi Women.

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Abstract:

Osteoporosis is a systematic bone disorder characterized by bone mass loss and bone tissue architectural degeneration. The incidence of osteoporosis in women increases with age, reflecting the considerable increase in bone loss rate in postmenopausal women once estrogen loses its protective influence. The purpose of this study was to determine the levels of osteocalcin, Vitamin D, and other parameters that influence bone quality and increased bone fragility in postmenopausal Iraqi women with T2DM. Current case control study included 89 postmenopausal women aged 50-70years old, 62 of them are T2DM patients and 27 controls. Ten of the T2DM patients were considered osteoporoticand 28 of them were considered osteopeniaand 22 werenormal, this classification according to the WHO criterion. After matchingfor body mass index (BMI) and age for patients and controls,results shows high significant difference in serum osteocalcin,vitamin D, and vitamin D binding protein levelsin patients compared to controls. In our study diabetic patients appear in high levels of osteocalcin, vit.D, and vitamin D binding protein compared with non-diabetic control. The processes underlying diabetes mellitus-induced skeletal problems are unknown. Anti-diabetic medications might have an adverse or favorable effect on bone metabolism. Osteoporosis is a prevalent condition among postmenopausal females. The study concludes that managing skeletal health in postmenopausal women entails screening fracture risk factors, lowering modifiable risk variables through dietary and lifestyle modifications, and using pharmacologic treatment for individuals at high risk of osteoporosis or fracture. Women with osteoporosis must be managed for the rest of their lives.

Key word: osteoporosis, type 2 diabetes, bone disease.

INTRODUCTION:

Osteoporosis is a systematic bone disease marked by a loss of bone mass and degradation of bone tissue architecture.The prevalence of osteoporosis in women increases with age which reflects the

significant increase in bone loss rate in postmenopausal women after losing the protective effect of estrogen. [1]

Osteocalcin, also known as bone Gla protein, is a marker for bone development.It induces insulin synthesis and enhances energy consumption and insulin sensitivity in target organs as a hormone.

Increased circulation levels of osteocalcin, especially by exogenous protein consumption, have been demonstrated in animal experiments to prevent obesity and glucose intolerance. Some epidemiological studies back up osteocalcin's involvement in maintaining human glucose and energy balance.

Monitoring Osteocalcin levels might help determine how well patients respond to therapy for metabolic bone disorders or anticipate bone losing in the postmenopausal women [2].

Numerous studies have demonstrated that the risk of fracture rises with the length of T2DM, poor glycemic control, and the presence of diabetic comorbidities[3].

Type 2 diabetes is caused by insulin resistance, a disease in which cells fail to utilize insulin efficiently, as well as insufficient insulin production, which is often associated with absolute insulin deficiency[4-7].

Individuals with T2DM, particularly those on hypoglycemic drugs and those with comorbidities such as neuropathy and retinopathy, are more prone to fall, leaving them more vulnerable to fractures. An increased incidence of fractures is also linked to hyperparathyroidism and renal osteodystrophy[8].

SUBJECTS AND METHODES:

Current case control study included 89 postmenopausal women aged 50 old, 62 of them are T2DM patients and 27 control. The study was conducted during the period from November 2020 to march 2021. A total of 90 postmenopausal women aged 50-70 years old were participated in the study. They were recruited from Medical City of Baghdad Teaching Hospital, educational laboratory and Al-Imamain Al-Kadhumain Medical City.

Among the studied postmenopausal women, 60 were T2DM patients and 30 controls. 10 of the T2DM patients were considered osteoporotic according to the WHO criterion: T-score less than -2.5 below the normal adult mean based on the establishedreference databases. And 28 of the patients were considered osteopenia as their T-score was between -2.5 and -1. And 22 patients who are T-score more than -1 were normal. Exclusion criteria included subjects who received osteoporosis therapy and vitamin D. Patients were diagnosed as osteoporosis and controls as normal by measuring bone mineral density (BMD), using dual energy x-ray absorptiometry (DXA) according to World Health Organization (WHO) diagnostic guidelines:

•T-score -1.0 or greater is “normal”.

•T-score between -1.0 and -2.5 is “osteopenia”.

•T-score -2.5 or below is “osteoporosis”.

Serum FBS measured by spectrophotometer, serum osteocalcin and insulin measured by enzyme linked immuno sorbent assay (ELISA) using kits manufactured by Sunlong /China.BMI and HOMA-IR were measured for patients and control. Data were analyzed using mean ± SD. Significance of difference was assessed using Student-t test for two independent means.

RESULTS:

Patients and controls were matching for age and body mass index (BMI),as shown in table (1), no significant difference appear between them.

Table (1): Mean Age and BMI for patients and control.

Parameters	Diabetic patients	Healthy control	p-value
BMI ,**Kg/m^2**	28.82±3.67	29.24±8.90	0.14
Age,Yrs.	62.09±4.43	60.40±4.22	0.55

The difference in serum osteocalcin level was significantly high in patients compared to that of controls (table 2).

Table (2): Mean value of biochemical parameters levels for patients and controls without osteopenia or osteoporosis.

parameters	Diabetic patients without osteopenia or osteoporosis	Healthy control without osteopenia or osteoporosis	p-value
FBS(mg/dl)	92.887±19.368	89.407±10.520	≤0.001
Insulin (mU/L)	6.11±0.40	5.56±0.17	0.02
Osteocalcin (ng/ml)	6.12±0.56	5.54±0.78	0.14
Spin T.score	-1.0±1.31	-0.73±1.41	0.39
Spin BMD	0.94±0.18	0.97±0.15	0.46
Vit.D (ng/ml)	25.71±2.39	21.78±2.42	≤0.001
HOMA-IR	2.82±1.36	1.24±0.25	≤0.001

In another way to classify patients and control according to t-score as shown in table (3) and table (4) osteopenia and osteoporosis.

Table (3): Mean value of biochemical parameters levels fordiabetic patients and controls withosteopenia.

parameters	Diabetic patients with osteopenia	Non diabetic control with Osteopenia	p-value
FBS(mg/dl)	81.343±15.372	101.437±26.521	0.007
Insulin (mU/L)	6.19±0.89	5.45±0.59	0.006
Osteocalcin(ng/ml)	6.17±0.90	4.88±0.96	0.007
Spin T.score	-1.29±0.62	-1.43±0.44	0.61
Spin BMD	0.89±0.14	0.90±0.05	0.78
Vit.D (ng/ml)	23.75±2.88	20.14±2.76	0.001
HOMA-IR	2.77±1.33	1.37±0.45	0.002

Table (4): Mean value of biochemical parameters levels for diabetic patients and controls with osteoporosis.

parameters	Diabetic patients with osteoporosis	Non diabetic control with Osteoporosis	p-value
FBS(mg/dl)	69.878±21.069	85.700±14.694	0.096
Insulin (mU/L)	5.49±0.39	5.60±0.61	0.76
Osteocalcin(ng/ml)	22.74±2.33	6.07±1.86	≤0.001
Spin T.score	-2.92±0.55	-2.76±0.50	0.65
Spin BMD	0.76±0.12	0.75±0.07	0.93
Vit.D (ng/ml)	22.74±2.33	21.38±2.53	0.34
HOMA-IR	2.06±0.89	1.19±0.27	0.14

DISCUSSION:

Diabetes mellitus is linked to poor bone health and an elevated risk of fracture,even if individuals have a normal or greater BMD. [9]. In our study diabetic patients appear in high levels of osteocalcin, vit.D, and insulin compared with non diabeticcontrol as shown in table (2).The processes underlying diabetes mellitus-induced skeletal problems are unknown. Anti-diabetic medications might have a negative or beneficial effect on bone metabolism. Thiazolidinedione, for example, increases bone loss and fracture risk by activating peroxisome proliferator-activated receptors (PPARγ) in bone marrow cells and inhibits osteoblastogenesis by decreasingWnt signaling pathways, Insulin-like Growth Factor-1 (IGF-1) and Runt-related transcription factor 2 (Runx2).Metformin and sulfonylureas, on the other hand, have a favorable or neutral effect on bone health and lower the risk of fracture, which explains our findings because this medicine was taken in our patients. The outcomes of preclinical and clinical investigations on the safety profile of insulin on bone health are contradictory. Incretin-based treatment (Dipeptidyl peptidase-4 (DPP-4) inhibitors and sodium-glucose transport protein -2 (SGLT2) inhibitors, as well as glucagon-like peptide-1 (GLP-1) receptor agonists,) are now available as anti-diabetic medications.While animal research imply that incretin-based medication has an anabolic impact on bone, limited human data on DPP-4 inhibitors and GLP-1 receptor agonists showed a neutral effect on bone health and fracture risk. Because of changes in calcium, phosphate, and sodium concentrations, SGLT2 inhibitors may induce

bone loss or increase fracture risk. As a result, anti-diabetic medication safety considerations are critical for diabetes mellitus therapy[10-12].

Most cases of osteoporosis have a somewhat connected bone formation and resorption process, but the resorption rate can far exceed the formation [13]. Osteocalcin is produced during the formation of bones and has a compact, calcium-dependent alpha helical shape in which the Gamma Carboxyglutamic Acid (GLA) residues bind to hydroxyapatite in the bone matrix and facilitate absorption. Bone mineralization occurs in this manner. In osteoporotic women, calcium and phosphorus deficits reduce the development of hydroxyapatite crystals, allowing free osteocalcinto circulate in the bloodstream[14],this were agree with the results in our study and may explain why osteocalcin levels in the serum of osteoporotic postmenopausal women are higher. On the other hand reduced estrogen concentrations during menopause result in decreased intestinal calcium absorption, leading in low serum calcium concentrations and accelerated osteoclastic resorption of bone, free osteocalcin in bloodstream,both enhance bone turnover and so contribute to the development of osteoporosis as risk factors [15].

Previous research indicated that osteocalcin, once undercarboxylated (unOC), acts as a hormone [16]and has a wide range of connections with glucose metabolism [17], fertility [18] and evenaging [19]. In Al-Daghri's study, the exact reason for thedecreased OC level in PMO cases remained unknown,this study disagree with our study,but interactions of OC with glucose metabolism mighthave an effect on the result since fasting glucose levelsin cases were slightly higher than control[20].

The link between T2DM and osteoporosis has been studied extensively, although the results are still inconclusive.

Diabetes may affect bone through a variety of methods, some of which may have opposing effects.

Obesity, which is common in T2DM, is closely linked to greater BMD, most likely as a result of mechanical loading and hormonal variables such as insulin, estrogen, and leptin.

Hyperinsulinemia has been linked to increased bone formation.

As a result, BMD may be affected by low insulin levels and the advancement of T2DM.In our study all groups revealed that there was non-significant difference in patients compared with control[21].

Increased blood glucose levels are known to interact with various proteins, resulting in a larger concentration of advanced glycation end-products (AGEs) in collagen, which may impair bone strength [22].Yamagishi et al[23]suggested that AGEs in collagen may react with bone to impair bone strength, leading to osteoporosis in diabetic individuals. Aggregated AGEs in the body may trigger osteoblast

apoptosis, resulting to a lack of bone production.[22],that explain our results in table (3),we can see that there was significant decrease in vit.D and significant increase in FBS, OC, insulin, and HOMA-IR in osteopenia diabetic patients. There is established evidence that Low vitamin D levels are not only linked to the development of T2DM, but also to the development of diabetic osteopenia due to altered vitamin D metabolism[22].

Vitamin D regulates parathyroid hormone (PTH) release, which is important for bone mineralization and calcium homeostasis [24].

Furthermore, diabetes' microvascular problems limit blood supply to the bones, which can lead to bone loss and fragility. Additional research is needed to identify whether diabetes is a main cause of osteoporosis or whether diabetes exacerbates osteoporosis, and whether osteoporosis should be considered one of the long-term consequences of diabetes. As a result, identifying and assessing populations at higher risk of developing osteoporosis is crucial for disease prevention and management[21]. For patients with T2DM, some authors have reported an elevated BMD [25-27],other studies have reported a decreased BMD[28, 29],and some have reported unaltered bone densitythat our results were agree with them [9, 30-32]. And some cross-sectional studies have even found normal BMD[33, 34].

CONCOLUSION:

Osteoporosis is a common illness in women following menopause. Managing bone health in postmenopausal women includes assessing fracture risk factors, decreasing modifiable risk variables through dietary and lifestyle changes, and employing pharmacologic therapy for patients at high risk of osteoporosis or fracture. Osteoporosis must be controlled for the remainder of a woman's life.

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