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# Comparative Study of Sclerostin and Lipid Profile in Type 2 Diabetic Patients of Iraqi Women with Osteoporosis

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## ABSTRACT

**Background:** Chronic hyperglycemia is the most frequent diabetes-related metabolic disorder because of faulty insulin action or production. According to the WHO, osteoporosis is a progressive systemic skeletal disorder that decreases bone mass and micro architecture bone tissue, increasing bone fragility and fracture risk. Nervosa damage determines how much a diabetic's body is damaged.

**Objective:** The current work aimed to examines age, BMI, HbA1c, fasting blood glucose, sclerostin, and lipid profiles (TC, TG, HDL-C, VLDL-C, and LDL-C) in Iraqi T2DM menopausal women with /without osteoporosis to detect biomarkers in such condition.

**Subjects and Methods:** 120 subjects were included in this study. They were divided into 3 groups; Group 1 (N = 40) consisted of seemingly healthy women, group 2 (N = 40) included type 2 diabetes patients without osteoporosis and group 3 (N = 40) included type 2 diabetes patients with osteoporosis. The patients were recruited from the Endocrinology and Diabetes Center of the Iraqi Ministry of Health in Baghdad between January and June 2022. The ages of participants ranged from 45 to 55 years. Glucose, HbA1c, sclerostin, and lipid profiles were measured. The t-test, mean, standard division, and other bio statistical approaches were used to examine the data.

**Results:** Various data were observed in osteoporosis patients with and without T2DM in Iraqi postmenopausal women regarding Sclerostin and other anthropometric parameters and biomarkers studied. **Conclusion:** Type 2 diabetic Iraqi women with and without osteoporosis had significantly lower Sclerostein levels than controls. Sclerostin correlates with BMI, HbA1c, FBG, and lipid profile (TC, TG, HDL-C, VLDL-C and LDL-C).

**Keywords:** T2DM, Sclerostin, Osteoporosis, HDL-C, BMI.

## INTRODUCTION

The term "chronic hyperglycemia" refers to the most prevalent metabolic disorder among people with diabetes mellitus. The culprit is either insulin synthesis, insulin action, or both of these mechanisms. Chronic hyperglycemia has been linked to ketoacidosis, nephropathy, high blood pressure, and foot issues. Numerous complementary and alternative therapies can be used to treat diabetes [(1,2)] . Diabetes mellitus, or DM, is one of the most ancient illnesses to impact people and is a metabolic disorder characterized by an increase in blood glucose levels, calls for close monitoring and efficient therapy. In addition to helping cells absorb glucose for energy, the hormone insulin, which is produced by pancreatic beta cells, also has a number of additional functions. A decrease in insulin production or sensitivity causes diabetes mellitus (DM) [(3)].

According to the World Health Organization, osteoporosis is a slowly progressing systemic skeletal condition marked by a decline in bone mass and the microstructural breakdown of bone tissue, which raises the risk of fracture (WHO).

Fractures occurred less commonly in premenopausal women than in postmenopausal women. According to the World Health Organization, osteoporosis is detected in postmenopausal women when their hip or spine bone mineral density (BMD) is two and a half standard deviations or more below the young adult mean (T-score = 2.5). There are conflicting opinions on how to detect osteoporosis in premenopausal women [(4)] . Osteoporosis is a condition where there is a loss of bone mass and mineral density, which makes bones more brittle and prone to fracture at modest forces. Fragility fractures occur when someone slides or falls, typically from a standing or seated posture. Hip, spine, and wrist fractures are the most common types of fragility fractures [(5)]. The protein sclerostin, which is produced by the SOST gene, controls bone growth by inhibiting the Wnt/-βcatenin signaling pathway. Genetic anomalies in the SOST gene can lead to sclerosteosis and Van Buchem disease. Both conditions differ in that blood sclerostin levels are undetectable or incredibly low, leading to considerable bone overgrowth [(6)]. Sclerostin, an osteoclast-secreted glycoprotein of 190 amino acids, is a potent inhibitor of osteoblastogenesis. Osteocytes release sclerostin, which travels through osteocyte canaliculi to the surface of the bone. There, it binds to the LRP5 and LRP6 co-receptors, which hinder co-localization with the frizzled protein and Wnt signaling, hence inhibiting osteoblastogenesis and bone formation [(7)].

## MATERIALS AND METHODS

The current study was conducted in the Endocrinology and Diabetes Center, Iraqi Ministry of Health, Baghdad. Three groups the first group (G1) consisted of 40 individual made up of participants in this study, each with an age range of 45 to 55 years.

The 40 people in the second group are type 2 diabetic' patients without osteoporosis, and the third group comprised forty individuals with type 2 diabetes and osteoporosis.



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5 ml venous blood were withdrawn from each participant, 3 ml were placed in a tube and left at room temperature for 30 minutes to coagulate, after which, serum was obtained via a centrifuge for 10 minutes at 3500 x g. The remaining portion of the blood (2 ml) was placed in a tube containing an anticoagulant (EDTA) for other measurements. Serum is used for the determination of biomarkers like FBS, HbA1c is measure with spectrophotometer, while sclerostin (Sclerostin ELISA Kit manufactured in USA by RayBiotech, Inc.) and, lipid profile (TC, TG, HDL-C, LDL-C and VLDL-C) were determined by enzymatic methods.

**Ethical approval:**

**The research approved by Endocrinology and Diabetes Center, Iraqi Ministry of Health's Ethics Committee and the College of Education for Pure Science / Ibn Al-Haitham – University of Baghdad. A consent document was signed by all those involved. The World Medical Association's Declaration of Helsinki was strictly adhered to in all human subjects' studies.**

***Statistical analysis***

The data were computed using the Student T-test, mean ± SD, and other findings were provided. The extraction P-value and post t-test were both utilized to show the difference between the groups with significance when the $P \leq 0.05$ in the test that compared the three study groups.

**RESULT**

In order to analyze the link between the three groups, 120 study participants were split into three groups: apparently healthy as controls (G1), people with type 2 diabetes mellitus (G2) without osteoporosis, and type 2 diabetic patients with osteoporosis (G3).

**Table (1)** described the correlation and the result of the comparison obtained.

BMI that was shown in the **same table and figure (1)** indicated a highly significant decrease in G1 (25.74 ± 3.35 kg/m$^2$) to G2 (30.26 ± 2.89 kg/m$^2$) and G3 (28.50 ± 3.39 kg/m$^2$), but also significant increase (P<0.005) as compared between G2 (30.26 ± 2.89 kg/m$^2$) to G3 (28.50 ± 3.39 kg/m$^2$). Regarding fasting blood glucose, **table (1) and figure (2)** showed a high significant value (P<0.001), when comparing between G1 (82.65 ± 5.77 mg/dl) and G2 (204.75 ± 56.72 mg/dl) and G3 (159.3 ± 28.86 mg/dl).

Also, a high significant (P<0.001) with increased level in G2 (204.75 ± 56.72 mg/dl) as compared to G3 (159.3 ± 28.86 mg/dl).

**Table (1):** Various markers obtained in postmenopausal T2DM women with/without osteoporosis

| Parameter | Apparently Healthy Control Group (G1) N = 40 | T2DM Group (G2) N = 40 | T2DM with Osteoporosis Group (G3) N = 40 | G1 Vs. G2 | G1 Vs. G3 | G2 Vs. G3 |
|---|---|---|---|---|---|---|
| BMI, kg/m$^2$ | 25.74 ± 3.35 | 30.26 ± 2.89 | 28.50 ± 3.50 | HS | HS | S |
| FBG, mg/dl | 82.65 ± 5.77 | 204.75 ± 6.72 | 159.3 ± 28.86 | HS | HS | HS |
| HbA1c% | 4.74 ± 0.43 | 8.64 ± 1.42 | 8.64 ± 1.39 | HS | HS | NS |
| Sclerostin | 741.97 ± 128.21 | 616.45 ± 81.76 | 471.55 ± 142.02 | HS | HS | HS |
| TC, mg/dl | 157.35 ± 23.22 | 230.25 ± 49.52 | 237.75 ± 55.69 | HS | HS | NS |
| TG, mg/dl | 130.27 ± 11.54 | 267.82 ± 58.50 | 203.92 ± 60.25 | HS | HS | HS |
| HDL-C, mg/dl | 50.74 ± 4.83 | 34.65 ± 1.29 | 38.85 ± 4.74 | HS | HS | HS |
| LDL-C, mg/dl | 124.64± 27.54 | 249.19 ± 50.18 | 237.30 ± 56.42 | HS | HS | NS |
| VLDL-C, mg/dl | 20.65 ± 2.30 | 53.65 ± 11.70 | 40.60 ± 12.22 | HS | HS | HS |

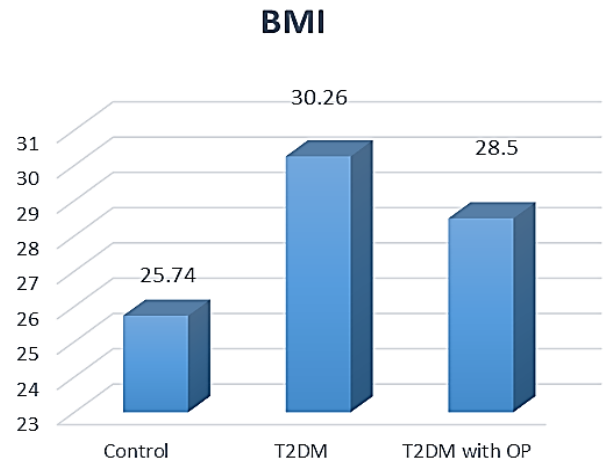


**Figure (1):** The mean ± SD of BMI levels for all studied groups.

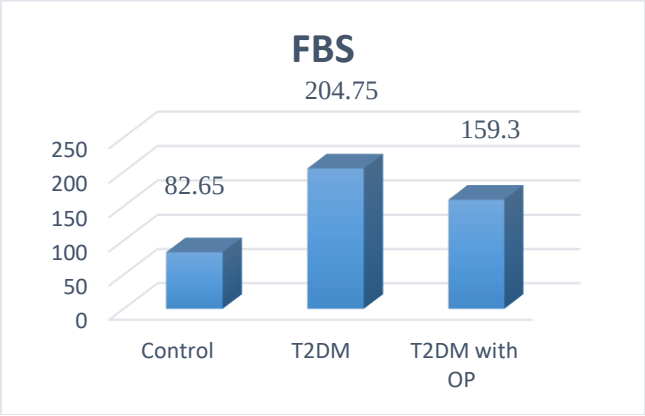


**Figure (2):** The mean ± SD of FBG levels for all studied groups.

Concerning HbA1c%, table (1) and figure (3) indicated a high significant decreased value (P<0.001) when comparing G1 (4.74 ± 0.43) with G2 (8.64 ± 1.42) and G3 (8.64 ± 1.39), but a non- significant result (P>0.005) when comparing G2 (8.64 ± 1.42) and G3 (8.64 ± 1.39).

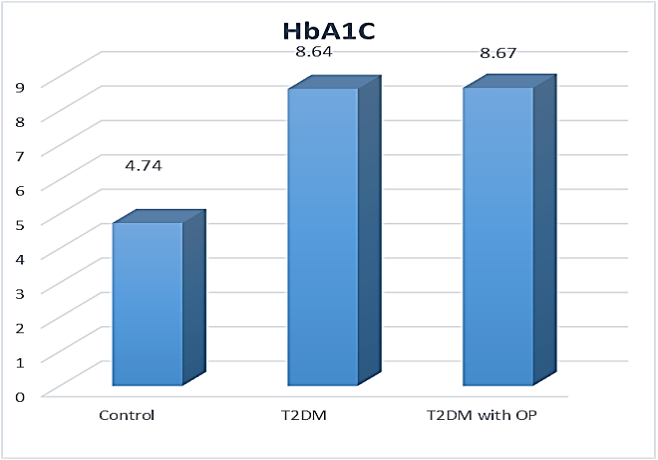


**Figure 3:** The mean ± SD of HbA1c% levels for all studied groups.

Regarding sclerostin, **table (1) and figure (4)** showed a high significant increase (P<0.001) when comparing G1 (741.97 ± 128.21) with G2 (616.54 ± 81.76) and G3 (471.55 ± 142.02), and a high significant increase (P<0.001) as compared G2 (616.54 ± 81.76) to G3 (471.55 ± 142.02).


**Figure (4):** The mean ± SD of Sclerostin levels for all groups studied

Regarding total cholesterol (TC), **table (1) and figure (5)** showed a significant decreased level in G1 (157.35 ± 23.22 mg/dl) as compared to G2 (230.25 ± 49.52 mg/dl) and G3 (237.75 ± 55.69 mg/dl). Also, G2 showed significant decrease (230.25 ± 49.52 mg/dl) as compared to G3 (237.75 ± 55.69 mg/dl).

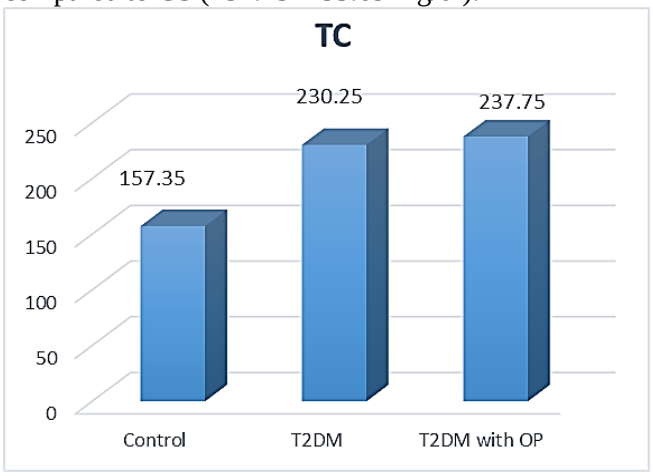


**Figure (5):** The mean ± SD of TC levels for all groups studied.

About TG, **table (1) and figure (6)** indicated a high significant decreased (P<0.001) in G1 (103.27 ± 11.54 mg/dl) as compared to G2 (267.82 ± 58.50 mg/dl) and G3 (203.92 ± 60.25 mg/dl). While there was a significant increase in G2 (267.82 ± 58.50 mg/dl) as compared to G3 (203.92 ± 60.25 mg/dl).

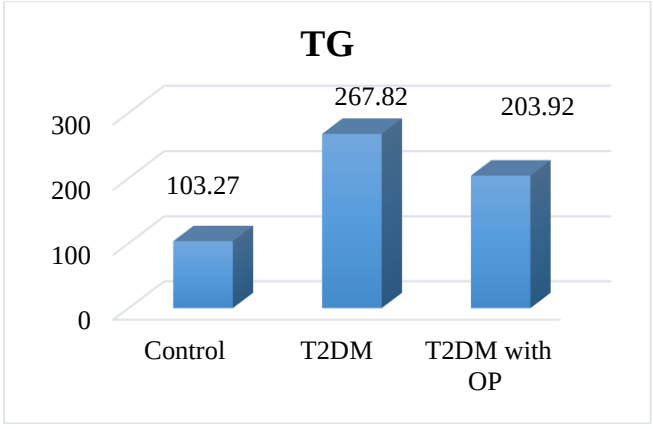


**Figure (6):** The mean ± SD of TG levels for all groups studied.

Regarding HDL-C, **table (1) and figure (7)** indicated a high significant increased levels (P<0.001) in G1 (50.75 ± 4.83 mg/dl) as compared to G2 (34.65 ± 1.29 mg/dl) and G3 (38.85 ± 4.47 mg/dl). While, there was a significant decrease in G 2 (34.65 ± 1.29 mg/dl) as compared to G3 (38.85 ± 4.47 mg/dl) (P < 0.001).

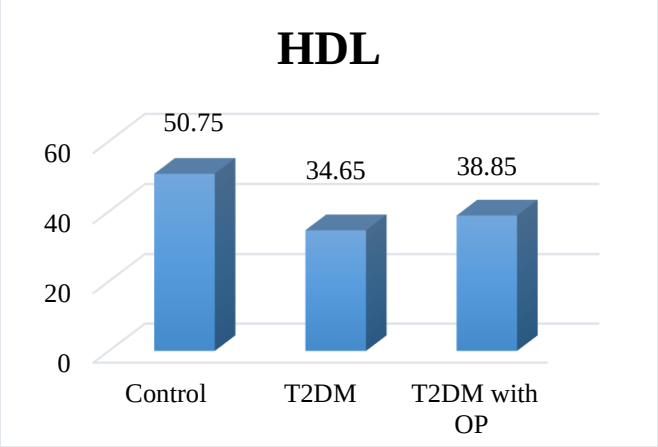


**Figure (7):** The mean ± SD of HDL-C levels for all groups studied.

Concerning LDL-C, **table (1) and figure (8)** indicated a high significant decreased level in G 1 (124.64 ± 27.54 mg/dl) as compared to G 2 (249.19 ± 50.18 mg/dl) and G 3 (237.30 ± 56.42 mg/dl). While, there was significant increase in G 2 (P<0.05) when compared to G 3 (237.3 ± 50.18 mg/dl) and G 1 (124.64 ± 27.54 mg/dl).

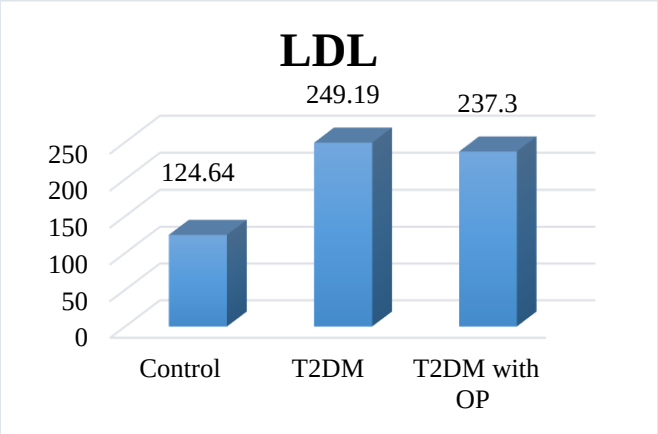


**Figure (8):** The mean ± SD of LDL-C levels for all groups studied.

As regards VLDL-C, table (1) and figure (9) indicated a high significant decreased value (P<0.001) in G 1 (20.65 ± 2.30 mg/dl) when compared to G 2 (53.65 ± 11.70 mg/dl) and G 3 (40.60 ± 12.22 mg/dl). While, there was a high significant increase in G 2 when compared G 1 (20.65 ± 2.30 mg/dl) and G 3 (40.60 ± 12.22 mg/dl).

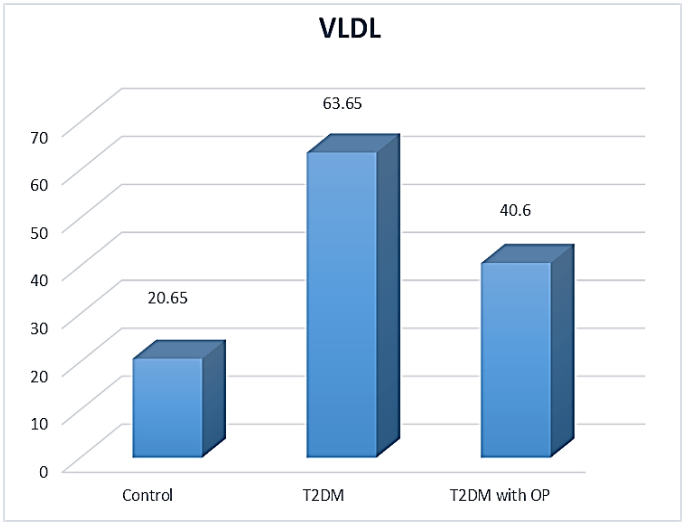


**Figure (9):** The mean ± SD of VLDL-C levels for all groups studied.

Table (2) showed the correlations between sclerostin with levels of BMI for G 2 and G 3 respectively where there were highly significant negative correlation (P ≤0.001) with G2 (r = -0.0102) and G 3 (r = -0.069)**,** while the correlations between sclerostin and FBG levels for G 2 and G 3 showed highly significant positive correlation (P ≤0.001) with G 2 (r = 0.1546) and G 3 (r = 0.097) respectively.

The other correlations studied between sclerostin and HbA1c% indicated a highly significant negative and positive correlation (P ≤0.00) for G 2 (r = -0.2122) and G 3 (r = 0.104) respectively. On the other hand, the correlations with TC showed highly significant negative and positive results (P ≤0.001) for G 2 (r = -0.0175) and G 3 (r = 0.0733) respectively, while the correlation with TG showed a highly significant positive correlation (P ≤0.001) for each of G2 (r = 0.1220) and G3 (r = 0.407).

The other correlations study performed between sclerostin with each of HDL-C and LDL-C; HDL-C showed highly significant negative and positive correlations (P ≤0.001) for G 2 (r = -0. 2424) and G 3 (r = 0.332), while LDL-C showed highly significant positive and negative correlation (P ≤0.001) for G 2 (r =0.0517) and G 3 (r = -0.015) respectively.

The correlations between sclerostin and the biomarker VLDL-C indicated a highly significant positive and negative correlations (P ≤0.001) for G 2 (r = 0.1220) and G 3 (r = -0.407) respectively.

**Table (2): The correlations between Sclerostin with various parameters studied: (BMI, FBG, HbA1c, TC, TG, HDL-C, LDL-C and VLDL-C)**

| Parameter | G2 T2DM | | G3 T2DM with Osteoporosis | |
|---|---|---|---|---|
| | r | p- value | r | p- value |
| BMI, kg/m$^2$ | -0.0102 | HS | -0.069 | HS |
| FBG, mg/dl | 0.1546 | HS | 0.097 | HS |
| HbA1c% | -0.2122 | HS | 0.104 | HS |
| TC, mg/dl | -0.0175 | HS | 0.0733 | HS |
| TG, mg/dl | 0.1220 | HS | 0.407 | HS |
| HDL-C, mg/dl | -0.2424 | HS | 0.332 | HS |
| LDL-C, mg/dl | 0.0517 | HS | -0.015 | HS |
| VLDL-C, mg/dl | 0.1220 | HS | -0.407 | HS |

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## DISCUSSION

Various studies regarding osteoporosis studies in postmenopausal women were investigated with and without another diseases such as T2DM [8, 9]. According to results obtained from the current study we noticed a highly significant decreased sclerostin levels for Iraqi women's with type 2 diabetes mellitus with and without osteoporosis when compared with control group, this may be due to aging and menopausal cycle. These variables led to abnormality in osteoblast and osteoclast as well as when progressed in diabetic due to osteoporosis and led to more decrease in sclerostin concentration. While, another study noticed a highly levels of sclerostin may be related with postmenopausal women and T2DM. Sclerostin levels and the risk of fracture may or may not be related. Higher sclerostin levels may be associated with a lower risk of fracture because of the strong relationship between sclerostin levels and bone mineral density (BMD). In another way, mature bone tissue with firmly implanted osteocytes produce sclerostin rather than early embedding osteoid osteocytes and juvenile osteocytes [10]. In line with the previous studies, sclerostin was decreased significantly in women with osteoporosis post-menopause. The Wnt pathway signaling, which regulates bone formation, is inhibited by sclerostin. Low levels of the circulating sclerostin protein lead to high bone mass. The researchers hypothesized that postmenopausal women with high sclerostin levels would be more susceptible to fractures caused by osteoporosis [11]. Previous studies performed by **Marzullo *et al.*** [12] showed that sclerostin was increased significantly in T2DM women postmenopausal with osteoporosis and hormones that control bone growth. In order to identify potential bone status modulators in obesity, we looked into the role of sclerostin and the premenopausal hormone status that controls it as a mechanism that promotes bone resorption**.** The studies have shown that sclerostin levels increase with aging, menopause, insulin resistance, and T2DM. The slight increase in sclerostin levels in postmenopausal women supports earlier findings that sclerostin levels grow gradually after menopause.

When it comes to sex steroids, testosterone has been found in both experimental and clinical trials to have the opposite impact of estrogen, which is known to increase circulation and bone sclerostin mRNA levels **[12].** In another study carried by **Zhao *et al.*** [13], which investigated that patient BMI values were significantly higher than those of the control group. This evidence is in line with other research that observed a connection between a higher BMI and high levels of insulin resistance, which in turn resulted in a reduction in insulin sensitivity to lower glucose levels in older persons. Also, a recent study observed that BMI in osteoporosis women postmenopausal was significantly high as compared to healthy women. An abrupt decline in bone mineral density and an uptick in inflammatory markers are indicators of rapid bone loss in postmenopausal osteoporotic women. In terms of BMI, there was no discernible difference between patients and controls [14], which is similar to the current results. Other investigators indicated that FBG was significantly elevated among T2DM patients and postmenopausal women and is an indicative of osteoporosis [15].

Aberrant glucose metabolism (AGM) in osteoporosis is usually identified using fasting glucose, which encompasses the normal, impaired fasting glucose (IFG), and diabetes mellitus (DM) guideline fasting glucose categories. Examining the relationship between the risk of osteoporosis and fasting glucose level may be useful in understanding how AGM influences the condition. However, nothing is known about how fasting glucose and osteoporosis are related. It is common practice to diagnose AGM, which includes IFG, impaired glucose tolerance (IGT), and DM, using fasting glucose and two hours following a load of glucose. Despite earlier research relating AGM and bone quality, the evidence currently available is insufficient to establish the impact of IFG on osteoporosis. Our study showed that IFG prevented osteoporosis and strengthened bones [15].

These findings are almost conclusive with others which observed that HbA1c was non–significantly between T2DM without osteoporosis and T2DM with osteoporosis. Higher blood glucose or HbA1c levels have been linked in a number of ways with an increased risk of reduced muscle mass, according to earlier studies. Insulin resistance and AGEs are the two main risk factors. Insulin resistance is a hallmark of T2DM, and it is linked to a number of inflammatory markers, such as IL-6, tumor necrosis factor alpha, and C-reactive protein (CRP). The synthesis and degradation of muscle proteins are both a part of muscle protein metabolism. The four primary proteolytic mechanisms that break down muscle protein are regulated by inflammatory signaling: Calpains, macrophage autophagy, and cell death are all ATP dependent ubiquitin proteasome activities [16].

In other study performed by **Kan *et al.*** [17] indicated that total cholesterol was highly significant in osteoporosis women and type 2 diabetes mellitus. The majority of the postmenopausal women in our study (82.5%) had T2DM as a chronic condition. These conditions were assumed to be related to lipids and osteoporosis. Numerous biological pathways can be used to account for the positive relationships between TC levels and BMD. However, the majority of studies investigating the link between lipids and osteoporosis relied on people who were typically in good condition. First, the researchers hypothesize that the nuclear hormone receptor peroxisome proliferator activated receptor γ (PPAR γ) may play a part in the relationship between lipid biomarkers and BMD. The PPAR γ gene can be activated by lipid metabolites. When PPAR γ levels increase, osteogenesis is inhibited, which causes more bone loss. Second, larger amounts of lipids are associated with more oxidized lipids and oxidative stress. The development of osteoblasts and adipocytes may be hampered or promoted by higher levels of oxidative stress.

This observation is in line with a lot of academic works by **Yamaguchi *et al.*** [18] in which triglycerides was non-signification between control women postmenopausal and osteoporosis. Malnutrition has the potential to induce or aggravate a wide range of disorders, including osteoporosis. Triglycerides were included as a potential variable in this study because blood lipid levels, particularly triglycerides, may be an indicator of nutritional status. Additionally, past studies on the connection between triglycerides and osteoporosis were contradictory. In a study with 214 postmenopausal women in Japan, lower TG was connected to a higher risk of vertebral fractures. However, a Korean analysis found no connection between serum lipid levels and BMD in postmenopausal women. Another study by **Tang *et al.*** [19] reported non-significantly in osteoporosis and control women to those of another study, which discovered that women with high HDL-C levels had a higher incidence of osteopenia or osteoporosis, suggesting that HDL-C levels may be a good indicator of osteopenia or osteoporosis. Through sex hormones, HDL-C, especially at high levels, affects BMD. Numerous studies have already established the significance of sex hormones like androgen and estrogen in preserving bone homeostasis.

Other result obtained by **Cui *et al.*** [20] indicated that serum levels of HDL-C levels was non-significantly in osteoporosis Iranian women's and found to be inversely correlated with BMD in postmenopausal women with inadequate vitamin D3 levels**.** Other studies related serum LDL-C levels indicated a significant result in osteoporosis postmenopausal women, which may be a significant factor, independent of bone markers, BMD, frailty, or use of medications for dyslipidemia. High serum LDL-C levels are equally as detrimental to bone and blood vessels as type 2 diabetes and chronic renal illness, despite the fact that they are known to be a risk factor for atherosclerosis and cardiovascular events. Our results and others investigated an inverse relationship between serum LDL-C levels and both radial and overall BMD. In their study that involved 355 Korean postmenopausal women, LDL-C was significantly lower in the highest quartile of blood LDL-C levels than in the lowest quartile.

Women with T2DM have increased capacity for producing and secreting very low density lipoprotein (VLDL) in fatty tissue than women without this type 2 of diabetes, suggesting that metabolic problems are caused by VLDL [21]. Other investigators indicated that VLDL has been increased significantly in postmenopausal women with osteoporosis as compared to healthy control. The VLDL was connected to vascular calcifications and bone loss in diabetic women. This demonstrates that the association between vascular calcifications and bone loss may be reflected in VLDL levels. Osteoporosis patients may have faster lipid metabolism than healthy controls, which could account for the low levels of VLDL particles. This could be connected to statins' impact on lipoprotein metabolism [22]. Also, other studies indicated that VLDL-C is significantly increased in women with osteoporosis when compared to without osteoporosis [23]. Most of diseases may correlated with genetic reasons, for that, The molecular technique (PCR) was recommended to applied in different medical field like diagnosis genetic disease ex: CML [24], Adenocarcinoma [25,26], and SARS-Cov-2 [27].

## CONCLUSION

According to results obtained from the present study we noticed highly significant decrease in concentration of sclerostin for Iraqi type 2 diabetic women's with and without osteoporosis when compared to control as well as we showed highly significant correlation when compared between sclerostin and BMI, HbA1c, FBG, lipid profile (TC, TG, HDL-C, VLDL-C and LDL-C). These changes could promote

diagnosis and can be utilized as confirming investigation for type 2 diabetic patients and may be predicators for development of osteoporosis.

## REFERENCES


1. **Al-Masoudi F , Bushra H (2021):** Evaluation of Nesfatin–1 and Other Biochemical Markers in diabetic Neuropathy Iraqi patients before and after treatment with tegretol. Annals of the Romanian Society for Cell Biology, 25 (4): 9422-9429.
2. **Salih N , Bushra H (2021):** Relation Study between Chromogranin a and Other Clinical Biomarker in Iraqi Children with Growth Hormone Deficiency Undergo Treated Via Recombinant Growth Hormone. Annals of the Romanian Society for Cell Biology, 25 (4): 11072-11077.
3. **Jaid H , Khaleel F, Salman I *et al.* (2022):** Evaluation of Insulin Resistance and Glutathione-S-transferase in Iraqi Patients with Type 2 Diabetes Mellitus and Diabetic Peripheral Neuropathy. Ibn AL-Haitham Journal For Pure and Applied Sciences, 35 (4): 194-205.
4. **Ahmed S (2022):** A study of Hepcidin levels and other Biochemical parameters in woman with Osteoporosis with Type 2 Diabetes Mellitus. Ibn AL-Haitham Journal for Pure and Applied Sciences, 35 (4): 183-193.
5. **Ha J , Choi E (2013):** Health perception, health concern, and health promotion behavior of the elders. Journal of Korean Gerontological Nursing, 15 (3): 277-285.
6. **De Maré A, Opdebeeck B, Neven E *et al.* (2022):** Sclerostin protects against vascular calcification development in mice. Journal of Bone and Mineral Research, 37 (4): 687-699.
7. **Silverman S (2010):** Sclerostin. Journal of Osteoporosis, 2010, 941419. https://doi.org/10.4061/2010/941419.
8. **Al-Kelabi H , Al-Tu'ma F, Al-Hasnawy T *et al.* (2022:** Al-Hasnawy, T. S. ; Al-Tu'ma, A. F. and Hussein, A. F. Association between 25(OH)D3 and Estrogens in Iraqi Postmenopausal Osteoporotic Women with Type 2 Diabetes. HIV Nursing, 22 (2): 628 – 643.
9. **Al-Obaidi H, Al-Tu'ma F, Al-Jawadi Z *et al.* (2022):** Al-Jawadi, A. A. M. and Al-Hasnawy, T. S. Comparative Study of Bone Specific Alkaline Phosphatase, Bone Mineral Density, and Zinc in Postmenopausal Osteoporosis in Iraqi Type 2 Diabetic Women. HIV Nursing, 22(2) : 644-652.
10. **Yamamoto M, Yamauchi M, Sugimoto T (2013):** Elevated sclerostin levels are associated with vertebral fractures in patients with type 2 diabetes mellitus. The Journal of Clinical Endocrinology & Metabolism, 98 (10): 4030-4037.
11. **Ardawi M, Rouzi A, Al-Sibiani S *et al.* (2012):** High serum sclerostin predicts the occurrence of osteoporotic fractures in postmenopausal women: the Center of Excellence for Osteoporosis Research Study.Journal of Bone and Mineral Research, 27 (12): 2592-2602.
12. **Marzullo P, Mele C, Mai S *et al.* (2021):** Obesity and bone loss at menopause: The role of sclerostin. Diagnostics, 11 (10): 1914. **https://doi.org/10.3390/diagnostics11101914**
13. **Zhao Q, Laukkanen J, Li Q *et al.* (2017):** Body mass index is associated with type 2 diabetes mellitus in Chinese elderly.Clinical interventions in aging, 12(1): 745-752.
14. **Jeedigunta Y, Sultana S, Kalashikam R *et al.* (2020):** Systemic Inflammation: A Risk Factor for Osteoporosis in Pre-and Post-menopausal Women.Journal of Womens Health and Development, 3 (4): 423-431.
15. **Park S, Jung J, Oh C *et al.* (2021):** Fasting glucose level and the risk of incident osteoporosis in the Koreans. Bone, 142: 115690. https://doi.org/10.1016/j.bone.2020.115690
16. **Fang L, Zhong S, Ma D *et al.* (2021):** A cross-sectional study: an assessment of low muscle mass and osteoporosis in type 2 diabetes mellitus patients with a high glycated hemoglobin level. https://doi.org/10.1177/20406223211026762
17. **Kan B, Zhao Q, Wang L *et al.* (2021):** Association between lipid biomarkers and osteoporosis: a cross-sectional study. BMC musculoskeletal disorders, 22 (1): 1-8.
18. **Yamaguchi T, Sugimoto T, Yano S *et al.* (2002):** Plasma lipids and osteoporosis in postmenopausal women. Endocrine journal, 49 (2): 211-217.
19. **Tang Y, Wang S, Yi Q *et al.* (2021):** High-density lipoprotein cholesterol is negatively correlated with bone mineral density and has potential predictive value for bone loss. Lipids in health and disease, 20(1): 1-17.
20. **Cui L, Shin M, Chung E *et al.* (2005):** Association between bone mineral densities and serum lipid profiles of pre-and post-menopausal rural women in South Korea. Osteoporosis International, 16 (12) : 1975-1981.
21. **Søndergaard E, Johansen R, Jensen M *et al.* (2017):** Postprandial VLDL-TG metabolism in type 2 diabetes. Metabolism, 75: 25-35.
22. **Värri M, Niskanen L, Tuomainen T *et al.* (2020):** Metabolite profiling of osteoporosis and atherosclerosis in postmenopausal women: a cross-sectional study. Vascular Health and Risk Management, 16: 515. doi: 10.2147/VHRM.S279028
23. **Afshinnia F, Shobha C, Tooraj Z (2007):** Association of lower serum cholesterol levels with higher risk of osteoporosis in type 2 diabetes. Endocrine Practice, 13 (6): 620-628.
24. **Ahmed A, Khaleel K, Fadhel *et al*, (2022):** Chronic Myeloid Leukemia: A retrospective study of clinical and pathological features. Bionatura. 7(3):41. DOI. 10.21931/RB/2022.07.03.41.
25. **Ali S, Lafta B, Al-Shammary A *et al*, (2021):** In vivo oncolytic activity of non-virulent newcastle disease virus Iraqi strain against mouse mammary adenocarcinoma. AIP Conference Proceedings, 2021, 2372, 030010.
26. **Ali S, Lafta B, Al-Shammary A *et al*, (2021):** Study the role of bacterial neuraminidase against adenocarcinoma cells in vivo. AIP Conference Proceedings, 2021, 2372, 030009.
27. **Rasoul L, Nsaif M, Al-Tameemi M *et al*. (2022):** Estimation of primer efficiency in multiplex PCR for detecting SARS-Cov-2 variants. Bionatura, 2022, 7(3). **http://dx.doi.org/10.21931/RB/2022.07.03.49.**