The Impact of Type 2 Diabetes Mellitus on the Markers of Osteoporosis (Sclerostin and CTRP3) in Postmenopausal Women: A Comparative, Observational, Study

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Abstract

Background

In the present study, our goal was to assess the impact of type 2 diabetes mellitus (T2DM) on osteoporosis markers (sclerostin and CTRP3) among postmenopausal women, and whether sclerostin and CTRP3 can be used as early biomarkers of osteoporosis/osteopenia in T2DM patients.

Methods

In a comparative, observation, study, a total of 30 postmenopausal women with osteoporosis/osteopenia and T2DM were included, as well as 30 non-diabetic women with osteoporosis/osteopenia. Thirty age and sex-matched healthy women were included as control groups. The enzyme-linked immunosorbent assay (ELISA) was used to assess the serum levels of sclerostin and CTRP3.

Results

A total of 90 women were included in the present study (30 patients per group). The serum CTRP3 was significantly lower in the DM-OST (3.45 ± 3.5 ng/dL) and OST (9.15 ± 3.65 ng/dL) groups than the control group (16.80 ± 0.55 ng/dL; p < 0.001); likewise, the serum sclerostin was higher in the DM-OST (109.95 ± 28.96 pmol/L) and OST (51.52 ± 23.18 pmol/L) than the control group (11.22 ± 1.21 pmol/L; p < 0.001). Notably, the serum CTRP3 was significantly lower and sclerostin was significantly higher in the DM-OST group than the OST group (p < 0.001)). In the DM + OST and OST groups, the serum CTRP3 correlated positively with BMD of lumbar spines, left femur, and left forearm. Serum CTRP3 was associated with lower risk of osteoporosis (OR) and diabetes (OR) in postmenopausal women. In addition, the serum sclerostin was associated with higher risk of osteoporosis (OR) and diabetes (OR) in postmenopausal women.

Conclusion

The present study provides a novel evidence about the impact of T2DM on osteoporosis biomarkers, serum CTRP3 and sclerostin. The results indicated that women with combined T2DM and osteoporosis/osteopenia exhibited more dysregulation in both biomarkers than women with osteoporosis/osteopenia alone. Thus, serum CTRP3 and sclerostin can be used as biomarkers for early detection of osteoporosis in diabetic patients.

1. Background

Over 422 million persons worldwide suffer from type 2 diabetes mellitus (T2DM) (1). T2DM is one of the most feared non-communicable diseases worldwide that substantially increase the risks of cardiovascular diseases, angiopathies, and various metabolic disorders (2). Osteoporosis is a common finding in diabetic patients, especially at-risk population such as postmenopausal women; about 40% of the elderly population with T2DM develop osteoporosis or some form of bone complications, with a higher risk in female patients(3). This association could emerge from the harmful skeletal effects of glucose toxicity, insulin resistance or deficiency, and the impacts of diabetes treatments, leading to defective bone mineral density (BMD) (4). T2DM is an established contributing
factor for accelerated deterioration of bony structure in osteoporotic patients; thus, it is imperative to detect early osteoporotic changes in at-risk patients, like diabetic, postmenopausal, women.

Around 70% of bone strength modified by BMD, which has a high genetic variance (5,6). All these variations leave the underlying pathogenesis of osteoporosis with no clear understanding(7). Nonetheless, it is well-known that loss-of-function mutations in osteoblasts co-receptors LRP5 lead to disorders associated with osteoporosis, which, in return, has brought more focus on the importance of Wnt ligands as a modifying factor in osteoporosis(8). Wnt ligands are glycoproteins that target LRP5 resulting in a cascade of events leading to the upregulation of gene expression (9). The regulation of Wnt ligands involves secreted antagonists, such as sclerostin -which usually expressed in osteocytes and late osteoblasts (10). The changes in the levels of circulating sclerostin may reflect the changes in bone activity, making it a promising biomarker for the diagnosis and prognosis of osteoporosis (11). However, previous studies presented controversial results of whether sclerostin has a positive or a negative correlation with osteoporosis (12–14).

Meanwhile, the adipose tissue plays a vital role in diabetes by secreting bioactive molecules called adipokines (15). The chronic low-grade inflammation mediated by adipokines shown to be potential biomarkers and therapeutic targets for DM complications (16). For instance, circulating levels of adiponectin show a decline in patients with T2DM (17). It is considered as the most beneficial adipokine in circulation, improving insulin sensitivity, endothelial functions, and inflammation (18). The C1q/TNF-Related Protein (CTRP) family is a paralogue of adiponectin (19). They share a favorable effect on inflammation, insulin sensitivity, and lipid metabolism (19). Several studies observed the association of CTRP family with diabetes, coronary artery diseases, metabolic syndrome, non-alcoholic fatty liver disease, and polycystic ovary syndrome (20–22). CTRP3 activates adenosine monophosphate-activated protein kinase (AMPK), thus enhancing insulin signaling and sensitivity (23). Studies reported that CTRP3 decline in insulin resistance, and rise after treatment with glucagon-like peptide-1 (GLP-1) receptor agonist (24). Recently, serum CTRP3 was found to be significantly associated with osteoporosis in postmenopausal women(25). Still, the serum CTRP3 has not been evaluated in diabetic patients with osteoporosis so far.

In the present study, our goal was to assess the impact T2DM on osteoporosis markers (sclerostin and CTRP3) among postmenopausal women, and whether sclerostin and CTRP3 can be used as early biomarkers of osteoporosis in T2DM patients.

2. Methods

2.1. Study design and Participants

We conducted a single-center, comparative, observational study through the period from June to December 2019. Three groups of patients were recruited from Department of Endocrinology and Metabolism of Al Zahraa University Hospital, Cairo, Egypt. In group 1 (DM + OST group), postmenopausal women were included if they had osteoporosis or osteopenia combined with T2DM. The diagnosis of osteoporosis was based on the findings of BMD, in which a T-score of less than 2.5 standard deviation (SD) was used as a cutoff value for the presence of osteoporosis; while a T-score ranging from −1 to -2.5 was used a definition of osteopenia. The diagnosis of T2DM was based on the criteria of the American Diabetes Association (ADA)(26). In group 2 (OST group), only non-diabetic, postmenopausal women with osteoporosis or osteopenia were included. In addition, sex and age-matched healthy women were included as control group. In all studied groups, menopause was identified through a history of menstruation
cessation for at least one year prior to study’s enrollment. The selection process of the participating women was done in non-probability, consecutive, sampling method.

We excluded women with morbid obesity, familial dyslipidemia, organ failure, malignancies, thyroid disorder, history of hormonal therapy, and/or associated immunological disorders.

### 2.2. Data collection

Every registered patient obtained the following information: age and sex, presentation of the condition, glucose and lipid levels in blood, comorbidities, and vitals. Also, the data collected included IR index assessment using Homeostatic Model Assessment (HOMA-IR), BMD scan findings, and blood CTRP3. In addition, we collected the anthropometric measures of the patients, insulin and sclerostin levels in serum, and HbA1c. The BMD was assessed through dual energy X-ray absorptiometry (Lunar Prodigy; General Electric Medical Systems; WI, USA) at the level of the femur neck and L2-L4 spines. Based on the various types of BMD, we grouped the participants into the usual BMD group, osteopenia group and osteoporosis group.

### 2.3. Biochemical Analysis

A 10 ml of venous blood was obtained from each participant after a 8-hour fasting for biochemical analysis. Each collected sample was split into two tubes of ethylenediaminetetraactic acid (EDTA); 7 ml for routine investigations. The other part was centrifuged for 10 minutes at 4000 rpm. Then it was stored at −80 ° C. The colorimetric enzymatic approaches used for estimation of the lipid profile and blood glucose profile. This procedure was done using Hitachi autoanalyzer 704 (Roche Diagnostics. Switzerland).

Automated Glycohemoglobin Analyzer (Tosoh Bioscience's HLC-723GX®, Tosoh, India) was used to estimate the HbA1c in blood. However, chemiluminescent immunoassay (Immulite2000, Siemens, Germany) was utilized to assess serum insulin form blood samples. The following calculator was used to estimate HOMA-IR: HOMA-IR = fasting insulin (IU/mL) × plasma glucose (mg/dL)/405[16].

Automated ELIZA (Thermo Scientific Finland, and computer program (ScanIt for Multiscan FC 2.5.1) was used to measure the serum levels of CTRP3. The device was set for CTRP3 sensitivity 0.38 ng/ ml. Also, the assay ranged from 0.63 ng/mL to 40 ng/ml and the CV% was less than 10%. However, sclerostin levels in serum were assessed utilizing quantitative sandwich ELISA by Biomedica (Vienna, Austria). These estimations were collected by picomoles per liter. The lower margin of identification was below 10 pmol/liter.

Basically, we tested two samples of certain concentrations for 6 times to estimate the variability between assays (4%). Also, we tested two samples of definitive concentrations in about three assays seeking the identification of inter-assay variability (3%).

### 2.4. Study Outcomes

Our primary objective was to compare the serum levels of sclerostin and CTRP3 between studied groups. Additional secondary outcomes were the correlations between studied biomarkers (sclerostin and CTRP3) and metabolic parameters of the included patients.

### 2.5. Statistical methods

Data analysis was conducted by SPSS software, version 22.0 (SPSS Inc., Chicago, Illinois, USA). Kolmogorov-Smirnov test was used to estimate the normal distribution of the continuous data. Descriptive statistics for continuous variables was based on mean and standard deviation (SD) in case of normal distribution and one-way
analysis of variance (ANOVA) with post-hoc test was used during the comparisons of these variables, while median with inter quartile range were used for presentation in case of there was no evidence of normality and the Mann-Whitney U test was used for comparison. The correlations were performed using spearman and Pearson’s correlation tests based on the normality. Categorical data was presented in numbers and percentages. The comparisons among categorical data were done using chi-square or Fisher’s exact tests. A probability value (P-value) of less than 5% was considered significant.

3. Results

A total of 90 women were included in the present study (30 patients per group) with comparable age (p = 0.1). Of the 60 patients with abnormal bone density, 33 patients (55%) had osteoporosis (Fig. 1).

The mean disease duration in diabetic group was 8.50 ± 6.64 years and the majority of the patients were on oral antidiabetics (56.7%). The mean systolic blood pressure was significantly higher in the DM + OST group than the OST group (125.33 ± 15.02 versus 112.33 ± 4.3 mmHg, respectively; p < 0.001). In addition, the mean body mass index (BMI) and waist circumference were significantly higher in DM + OST group than the OST and control groups (p < 0.001). With regard to lipid profile, the mean LDL was significantly higher in the DM + OST and OST groups than the control group; while the mean HDL was lower the DM + OST and OST groups than the control group (p < 0.001). Patients with combined T2DM and osteoporosis had significantly higher serum triglyceride and cholesterol than patients with osteoporosis alone (p < 0.001). The blood glucose profile parameters were similar in the OST and control groups (p > 0.05), except for HOMA-IR and serum insulin which were significantly lower in the OST group (p = 0.09 and 0.034, respectively; Table 1).

With regard to DEXA findings, the results showed that the mean BMD of lumbar spines, left femur, and left forearm were significantly lower in the OST group than the DM + OST group and control groups (p < 0.001). The same parameters were significantly higher in the DM-OST group than the control group (p < 0.001; Table 2).

The serum CTRP3 was significantly lower in the DM-OST (3.45 ± 3.5 ng/dL) and OST (9.15 ± 3.65 ng/dL) groups than the control group (16.80 ± 0.55 ng/dL; p < 0.001); likewise, the serum sclerostin was higher in the DM-OST (109.95 ± 28.96 pmol/L) and OST (51.52 ± 23.18 pmol/L) than the control group (11.22 ± 1.21 pmol/L; p < 0.001). Notably, the serum CTRP3 was significantly lower and sclerostin was significantly higher in the DM-OST group than the OST group (p < 0.001); Figs. 2 and 3).

In the DM + OST group, the serum CTRP3 correlated positively with BMD of lumbar spines, left femur, and left forearm. In addition, the serum CTRP3 correlated significantly with serum insulin (r = 0.612; p = 0.009) and BMI (r = 0.372; p = 0.043). On the other hand, the serum sclerostin correlated negatively with BMD of lumbar spines, left femur, and left forearm. The serum sclerostin also correlated significantly with HOMA-IR (r = -0.732; p < 0.001), HbA1c (r = -0.307; p = 0.049), and waist circumference (r = 0.322; p = 0.037). Similarly, both serum CTRP3 and sclerostin correlated significantly with BMD parameters, HOMA-IR, HbA1c, LDL, and HLD levels (Table 3).

4. Discussion

While the current published literature demonstrates significant association between the serum sclerostin and CTRP3 with osteosclerosis, little is known about the additional impact of T2DM on these biomarkers. In our study, we demonstrated that the presence of T2DM in osteoporotic/osteopenic women led to further reduction in the serum CTRP3 than the presence of osteoporosis again. The serum CTRP3 was negatively correlated with higher degrees of
osteoporosis/osteopenia as indicated by BMD as well as markers of insulin resistance and glycemic control. On the other hand, serum sclerostin exhibited further upregulation in patients with combined T2DM and osteoporosis/osteopenia than osteoporosis/osteopenia only; the biomarker was positively correlated with higher degrees of osteoporosis as indicated by BMD as well as markers of insulin resistance and glycemic control. The multivariate regression analysis demonstrated that serum CTRP3 and sclerostin were independent predictors of T2DM in women with osteoporosis/osteopenia.

CTRP3, a member of adipocytokines-related family, is a critical regulator of many cellular processes that mediate metabolism, development, and inflammation. A cumulative body of evidence indicated that dysregulation of serum CTRP3 levels is a constant feature of many metabolic disorders, including diabetes and obesity (20–22). Recently, an emerging evidence highlighted a significant role of serum CTRP3 in regulation of bone hemostasis; the role of CTRP3 in regulation of bone structure appears to stem from its ability to maintain normal turnover of chondrocytes and cartilaginous structure through regulation of ERK1/2 and PI3K pathways (27,28). Thus, authors has linked downregulation of serum CTRP3 to defective bone metabolism and features of osteoporosis (29). On the other hand, the association between CTRP3 and T2DM is well-established with reported decline in serum CTRP3 levels among cases with insulin resistance and poor glycemic control(24). Therefore, we hypothesized that serum CTRP3 can be used as a biomarker for detection of early osteoporosis in patients with T2DM patients. Our analysis demonstrated that the serum CTRP3 exhibited higher decline in the setting of combined T2DM and osteoporosis than osteoporosis alone. The serum CTRP3 was independent predictors of T2DM in women with osteoporosis and correlated significantly with metabolic parameters. To our knowledge, this is the first report that addressed the impact of T2DM on serum CTRP3 among women with osteoporosis. Nonetheless, the association between serum CTRP3 and osteoporosis or T2DM alone were reported previously. For example, Xu and colleagues (25) reported significant decline in serum CTRP3 among postmenopausal women with osteoporosis. Other reports showed significant decline in serum CTRP3 among patients with T2DM and diabetic nephropathy (30,31).

Sclerostin is usually secreted by osteocytes and late osteoblasts to mediate physiological bone metabolism (10). The changes in the levels of circulating sclerostin may reflect the changes in bone activity, making it a biomarker for the diagnosis and prognosis of osteoporosis (11). On the other hand, previous animal models demonstrated high expression of sclerostin gene, SOST, in the setting of T2DM(32). Thus, it is logical to assume higher degree of dysregulated levels of sclerostin in patients with combined T2DM and osteoporosis. We found that serum sclerostin was higher in patients with combined T2DM and osteoporosis than osteoporosis only; the biomarker was positively correlated with higher degrees of osteoporosis- as indicated by BMD- as well as markers of insulin resistance and glycemic control. Similar to our findings, Wang and colleagues (33) showed that the combination of T2DM and osteoporosis led to higher increase in serum sclerostin than osteoporosis alone; moreover, serum sclerostin correlated with BMD parameters, HbA1c, and serum glucose level. Likewise, García-Martín and colleagues (34) found positive correlation between with higher severity of osteoporosis, HOMA-IR, and serum insulin.

Despite the novelty of the present study, we acknowledge the presence of some methodological limitations. The cross-sectional nature of the present study limits the validity of the observed associations and further long-term studies are still needed to confirm the sequential role of T2DM on osteoporosis biomarkers. In addition, the lack of pre-planned samples size calculation and being a single-center experience are additional limitations of the present study.

In conclusion, the present study provides a novel evidence about the impact of T2DM on osteoporosis biomarkers, serum CTRP3 and sclerostin. The results indicated that women with combined T2DM and osteoporosis/osteopenia...
exhibited more dysregulation in both biomarkers than women with osteoporosis/osteopenia, alone. Thus, serum CTRP3 and sclerostin can be used as biomarkers for early detection of osteoporosis in diabetic patients. Further experiments are warranted to confirm our findings and to understand the mechanistic processes behind the additional impact of T2DM on the osteoporosis biomarkers. In addition, further investigations about the link between adipose tissue and bone hemostasis are recommended.

**Abbreviations**

BMI: Body mass index

CTRP3: C1q/TNF-Related Protein

HbA1c: Glycated hemoglobin

HOMA-IR: Homeostatic Model Assessment

GLP-1: Glucagon-like peptide-1

OR: odds ratio

T2DM: Type 2 diabetes mellitus

**Declarations**

**Ethics approval and consent to participate**

The study was approved by responsible ethics committee of Al Zharaa University Hospital (IRB No). Written informed consent was obtained from every eligible patient women prior to the study’s enrollment.

**Consent for publication**

Not applicable

**Availability of data and materials**

Not applicable

**Competing interests**

The authors declare that they have no competing interests

**Funding**

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**Authors' contributions**

IH developed the study design, shared in data collection, interpreted the data, and revised the manuscript; MA developed the study design, shared in data collection, interpreted the data, and revised the manuscript; KB shared in data collection, analyzed and interpreted the data, and revised the manuscript; MB shared in data collection,
analyzed and interpreted the data, and revised the manuscript; SH shared in data collection, analyzed and interpreted the data, and revised the manuscript; JK shared in data collection and manuscript writing; NS shared in data collection and manuscript writing; CF shared in data collection and manuscript writing. All authors have read and approved the manuscript.

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Tables

Table (1): Comparison between groups according to demographic and laboratory data.
| Parameters | Groups | ANOVA | Post HOC test |
|------------|--------|-------|---------------|
|            | Control (n=30) | DM +OST (n=30) | OST Only (n=30) | p-value | I vs. II | I vs. III | II vs. III |
| Age (years) | Mean±SD | 57.73±1.98 | 53.40±7.69 | 56.10±1.54 | 0.102 | 0.301 | 0.179 | 0.328 |
|            | Range   | 55_60 | 33_65 | 55_60 | | | | |
| SBP        | Mean±SD | 116.67±7.11 | 125.33±15.02 | 112.33±4.30 | <0.001** | <0.001** | 0.094 | <0.001** |
|            | Range   | 110_130 | 110_150 | 110_120 | | | | |
| DBP        | Mean±SD | 75.33±5.07 | 81.33±10.08 | 73.67±4.90 | <0.001** | 0.002* | 0.366 | <0.001** |
|            | Range   | 70_80 | 70_100 | 70_80 | | | | |
| BW         | Mean±SD | 71.87±18.10 | 84.93±13.33 | 74.50±8.32 | <0.001** | <0.001** | 0.463 | 0.004* |
|            | Range   | 53_95 | 70_112 | 65_89 | | | | |
| Ht         | Mean±SD | 161.40±4.68 | 159.23±6.89 | 160.07±4.55 | 0.308 | 0.129 | 0.348 | 0.557 |
|            | Range   | 154_168 | 147_170 | 151_166 | | | | |
| BMI        | Mean±SD | 27.54±6.74 | 33.48±4.56 | 29.09±3.03 | <0.001** | <0.001** | 0.234 | <0.001** |
|            | Range   | 20.3_36.6 | 25.2_41.6 | 23.6_34.3 | | | | |
| WC         | Mean±SD | 100.27±14.45 | 111.40±8.11 | 103.07±8.21 | <0.001** | <0.001** | 0.313 | 0.003* |
|            | Range   | 84_130 | 97_131 | 95_116 | | | | |
| HC         | Mean±SD | 117.27±15.55 | 120.07±9.37 | 115.13±7.85 | 0.25 | 0.345 | 0.471 | 0.098 |
|            | Range   | 85_141 | 100_134 | 101_126 | | | | |
| WHR        | Mean±SD | 0.86±0.09 | 0.93±0.05 | 0.90±0.05 | <0.001** | <0.001** | 0.045* | 0.047* |
|            | Range   | 0.75_0.99 | 0.82_1 | 0.83_0.97 | | | | |
| FBS        | Mean±SD | 93.60±6.65 | 206.97±67.98 | 89.20±8.01 | <0.001** | <0.001** | 0.669 | <0.001** |
|            | Range   | 79_100 | 110_328 | 75_98 | | | | |
|   | PPBS       |   | HbA1c       |   | CHO         |   | TG          |   | HDL         |   | LDL         |   | INS         |   | VD          |   | HOMA        |
|---|------------|---|-------------|---|-------------|---|-------------|---|-------------|---|-------------|---|-------------|---|-------------|
|   | Mean±SD    |   | Range       |   | Mean±SD     |   | Range       |   | Mean±SD     |   | Range       |   | Mean±SD     |   | Range       |   | Mean±SD     |   | Range       |
|   | 122.53±11.51 |   | 107_138     |   | 5.13±0.27   |   | 4.6_5.4     |   | 41.47±2.54  |   | 39_47       |   | 2.11±0.57   |   | 13.5_18.4   |   | 2.11±0.57   |   | 1_2.9       |
|   | 261.67±87.99|   | 130_404     |   | 8.96±2.00   |   | 6.3_13.6    |   | 38.70±5.75  |   | 31_53       |   | 6.56±2.07   |   | 7.4_13.8    |   | 6.56±2.07   |   | 3.5_11.5    |
|   | 122.20±11.72|   | 108_139     |   | 5.39±0.25   |   | 4.9_5.6     |   | 36.90±6.40  |   | 31_54       |   | 1.52±0.40   |   | 13.3_15.6   |   | 1.52±0.40   |   | 1.1_2.3     |
|   | 261.67±87.99|   | 130_404     |   | 5.39±0.25   |   | 4.9_5.6     |   | 36.90±6.40  |   | 31_54       |   | 1.52±0.40   |   | 13.3_15.6   |   | 1.52±0.40   |   | 1.1_2.3     |
|   | <0.001**   |   | <0.001**    |   | <0.001**    |   | <0.001**    |   | <0.001**    |   | 0.98        |   | <0.001**    |   | <0.001**    |   | <0.001**    |
|   | <0.001**   |   | <0.001**    |   | <0.001**    |   | <0.001**    |   | <0.001**    |   | 0.382       |   | <0.001**    |   | <0.001**    |   | <0.001**    |
|   | 0.98       |   | 0.382       |   | 0.134       |   | 0.213       |   | 0.182       |   | 0.008*      |   | 0.009*      |   | 0.006*      |   | 0.042*      |
|   | <0.001**   |   | <0.001**    |   | <0.001**    |   | <0.001**    |   | <0.001**    |   | 0.042*      |   | <0.001**    |   | <0.001**    |   | <0.001**    |
|   | <0.001**   |   | <0.001**    |   | <0.001**    |   | <0.001**    |   | <0.001**    |   | 0.034*      |   | <0.001**    |   | <0.001**    |   | <0.001**    |

**Table (2):** Comparison between groups according to DEXA, t-AP spine, and lt. femur and lt. forearm.
| DEXA | Groups | ANOVA | Post HOC test |
|------|--------|-------|---------------|
|      | Control (n=30) | Osteoporotic diabetic group (n=30) | Non diabetic osteoporotic group (n=30) | F | p-value | I vs. II | I vs. III | II vs. III |
| Normal | 30 (100%) | 0 (0%) | 0 (0%) | $x^2=42.633$ | <0.001** | <0.001** | <0.001** | 0.349 |
| Osteopen | 0 (0%) | 12 (40%) | 15 (50%) | | | | | |
| Osteopor | 0 (0%) | 18 (60%) | 15 (50%) | | | | | |

**t-AP spine**

| Mean±SD | -0.14±0.98 | -1.85±1.51 | -2.43±0.64 | 34.893 | <0.001** | <0.001** | <0.001** | 0.044* |
| Range | -1.2 | -4.1 | -3.5 | -1.7 |

**Lt.femur**

| Mean±SD | 0.45±0.95 | -1.06±1.10 | -1.30±0.81 | 29.204 | <0.001** | <0.001** | <0.001** | 0.336 |
| Range | -0.2 | -4.7 | -2.4 | 0 |

**Lt.forearm**

| Mean±SD | 1.55±2.36 | -2.27±1.65 | -1.70±0.93 | 41.856 | <0.001** | <0.001** | <0.001** | 0.207 |
| Range | 0.3 | -5.9 | -3.1 | -0.6 |

*Using: One Way Analysis of Variance/ $x^2$: Chi-square test*

$p$-value>0.05 NS; *$p$-value <0.05 S; **$p$-value <0.001 HS

**Table (3):** Correlation between DEXA, CTRP3 and sclerostin with all parameters, using Pearson Correlation Coefficient in Osteoporotic diabetic group.
| Osteoporotic diabetic group | DEXA  | CTRP3    | Sclerost. |
|----------------------------|-------|----------|-----------|
|                            | r     | p-value  | r         | p-value   | r         | p-value   |
| Age (years)                | 0.421 | 0.020*   | 0.369     | 0.045*    | 0.095     | 0.619     |
| Disease duration           | 0.031 | 0.870    | -0.302    | 0.105     | -0.009    | 0.964     |
| SBP                       | 0.203 | 0.283    | 0.369     | 0.045*    | 0.171     | 0.367     |
| DBP                       | 0.247 | 0.188    | 0.328     | 0.037*    | 0.132     | 0.487     |
| BW                        | 0.120 | 0.526    | 0.372     | 0.043*    | 0.097     | 0.610     |
| Ht                        | 0.390 | 0.033*   | 0.262     | 0.036*    | 0.171     | 0.366     |
| BMI                       | -0.092| 0.630    | 0.260     | 0.166     | 0.004     | 0.983     |
| WC                        | 0.109 | 0.565    | 0.140     | 0.460     | 0.322     | 0.037*    |
| HC                        | 0.117 | 0.539    | 0.156     | 0.410     | 0.045     | 0.814     |
| WHR                       | -0.018| 0.923    | -0.011    | 0.954     | 0.270     | 0.048*    |
| FBS                       | -0.537| 0.002*   | 0.137     | 0.470     | -0.205    | 0.277     |
| PPBS                      | -0.455| 0.012*   | 0.013     | 0.947     | -0.131    | 0.490     |
| HbA1c                     | -0.398| 0.029*   | 0.010     | 0.957     | -0.307    | 0.049*    |
| CHO                       | -0.410| 0.024*   | -0.112    | 0.554     | -0.075    | 0.693     |
| TG                        | 0.089 | 0.640    | 0.121     | 0.525     | 0.059     | 0.757     |
| HDL                       | 0.005 | 0.980    | 0.060     | 0.753     | -0.106    | 0.577     |
| LDL                       | -0.387| 0.035*   | -0.232    | 0.217     | 0.012     | 0.951     |
| INS                       | 0.116 | 0.658    | 0.612     | 0.009*    | -0.286    | 0.265     |
| VD                        | -0.370| 0.044*   | 0.338     | 0.038*    | -0.086    | 0.652     |
| HOMA                      | -0.307| 0.230    | 0.046     | 0.859     | -0.732    | <0.001**  |

r-Pearson Correlation Coefficient

p-value > 0.05 NS; *p-value < 0.05 S; **p-value < 0.001 HS