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Vitamin D Status In Postmenopausal Saudi Women With Type 2 Diabetes Mellitus In Relation To Indices Of Bone Health.

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ABSTRACT

Vitamin D is involved in glucose homeostasis and in the mechanisms underlying insulin release. Vitamin D deficiency increases the risk of many diseases, including type 2 diabetes and osteoporosis. Serum 25-hydroxy vitamin D (25-OH-D) is an important determinant of bone health. We assessed vitamin D status in postmenopausal diabetic and non-diabetic Saudi women and determined the incidence of low bone mineral density (BMD) in relation to bone mass index (BMI) and bone turnover markers (BTMs). Postmenopausal Saudi women (n 98) aged 50–80 years living in Jeddah, Saudi Arabia were divided into diabetic (n=53) and non-diabetic (n=45) groups. Serum levels of intact parathyroid hormone (IPTH), 25-OH-D, glucose, insulin and BTMs were measured. BMD was measured by dual-energy X-ray absorptiometry (DEXA) at the lumbar spine, total hip and femur neck. We observed that 86.0% of the diabetic group and 81% of the non-diabetic group were vitamin D-deficient [25-OH-D <50.0 nmol/L (20 ng/ml)]. The BMD at lumbar spine was significantly lower in diabetic overweight (0.96±0.13 g/cm2) compared to diabetic obese (1.05±0.17 g/cm2) p = 0.05, and significantly lower in non-diabetic overweight (0.93±0.14 g/cm2) compared to diabetic obese (1.05±0.17 g/cm2) p = .013. The women were further divided into four subgroups according to their diabetes diagnosis and BMI ≥30 Kg/m2 for obese, and BMI 25-29.9 Kg/m2 for overweight. Serum 25-OH-D level was inversely related to PTH in diabetic obese. BMD at lumbar spine in non-diabetic obese was significantly positively correlated with BMI and with 25-OH-D in the same subgroup. Markers of bone turnover (osteocalcin (OC) and C-terminal telopeptide (CTx) were significantly negatively correlated with 25-OH-D in both the diabetic overweight and non-diabetics overweight. In conclusion, low vitamin D levels contribute to osteoporosis and diabetes complications in postmenopausal Saudi women, and the effects of vitamin D on cortical bone were different from the effects on cancellous bone. The BMD results suggested that osteoporosis was more common among these diabetic women and certainly warrants further investigation.

Keywords: Vitamin D; Bone mineral density (BMD); Postmenopausal Saudi women; Osteoporosis; Type 2 diabetes mellitus.

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INTRODUCTION

Vitamin D functions are not limited to bone heath, it may involve in the promotion of insulin secretion and insulin sensitivity (1). The serum concentration of 25-hydroxy-vitamin D is usually used to determine vitamin D status (2). It reflects vitamin D produced in the skin as well as that acquired from the diet. Results of general population studies indicate that poor vitamin D status, characterized by low serum 25-OHD3 levels, is associated with a higher prevalence chronic heart failure, hypertension, and hyperparathyroidism and were related to type II diabetes in humans and osteoporosis (3). Serum 25-hydroxyvitamin D was found to have a positive association with BMD. The main source of vitamin D is the cutaneous production through sunlight, which is influenced by the time of day, season and latitude. The dietary intake of vitamin D, however, also plays a role in the development and maintenance of an adequate BMD. The incidence of type 2 diabetes mellitus (type 2 DM) is increasing at an alarming rate both nationally and worldwide. Diabetes type 2 is a metabolic disorder that is primarily characterized by insulin resistance, and altered insulin secretion and hyperglycaemia. Patients with diabetes have multiple skeletal disorders, including osteopenia and osteoporosis (4). Demonstrated that diabetes mellitus could be associated with a loss of bone mass leading to osteoporosis. This finding has since received a great deal of attention and been investigated by a number of researchers. Therefore, the focus of this thesis will be on the determination of the status of vitamin D and indices of bone health, in postmenopausal Saudi women with type2 diabetes.

MATERIAL AND METHODS

Subjects

Total of 98 women aged 50-80 were divided into 53 diabetic and 45 non-diabetic.

Further subdivided into four subgroups according to their diabetes diagnosis and BMI: 35 diabetic obese; 18 diabetic overweight; , 25 non-diabetics obese, and 20 non-diabetics overweight.

Assessments of vitamin D status, PTH and insulin

Serum 25-OH-D, PTH and insulin were measured by direct competitive and a direct sandwich chemiluminescence immunoassays using LIASON autoanalyzer, (DiaSorinInc, Stillwater, MN, USA).

Serum intact-OC, CTX were measured using ECLIA Elecsysautoanalyzer [Roche Diagnostics GmbH, D-68298 Mannheim, Germany].

Assessments of Bone Mineral Density

All subjects were undergo BMD measurement at the lumbar spine (L1- L4) and femoral neck (right and left) using Dual Energy X-ray absorptiometry (DXA)(Lunar iDXA, GE Healthcare, United Kingdom).

Statistical Analysis

All statistical analyses were performed using the Statistical Package for Social Sciences (SPSS) version 17.0 (SPSS Inc., Chicago, IL, USA). Results that were not normally distributed were statistical by nonparametric test. The data from diabetic and non-diabetic were expressed as mean ± SD.

One-way ANOVA was performed to compare the mean between subgroups based on case-control study. Associations between continuous variables were examined using Pearson correlation coefficient Statistical significance was defined as the probability of $P \leq 0.05$ (two-sided).

RESULTS

The subjects' Anthropometrics parameters are shown in Table 1 for 53 postmenopausal diabetic women and for the 45 postmenopausal non- diabetic women. The mean body mass index BMI for the diabetic patients was (34.57 Kg/m2) and (32.07 Kg/m2) for the women non-diabetes, these women were considered obese class I for the two groups. The mean ± SD of WHR in diabetic group was 0.94 ± .11 and 0.86 ± .08 in the

group of women non-diabetes. The duration of diabetes mellitus was significantly lower in diabetic obese compered to diabetic overweight women p= 0.050. The BMI was significantly lower in diabetic overweight (26.19±2.03 Kg/m2, p = .000) and non-diabetic overweight (27.16±1.97 Kg/m2, p = .000) compered to diabetic obese (37.60±4.65 Kg/m2) and there was no significant deference between diabetic obese and non-diabetic overweight (p = .06). Table 1 displays Vitamin D status, PTH, BTMs in postmenopausal Saudi women with or without diabetic. As a shown there was no statistically significant difference between groups as determined by one-way ANOVA (p > .05) for intact parathyroid hormone, octeocalcin, serum-cross linked C-terminal telopeptide of type 1 collagen. The level of 25-OHD trend to significantly among different group (p = .062)

Table 1: Clinical characteristics, serum concentrations of; vitamin D, glucose, insulin, Bone turnover marker and BMD in the study groups

Variable	Diabetic obese (n=35)	Non-diabetic obese (n=25)	Diabetic overweight (n=18)	Non-diabetic overweight (n=20)	ANOVA (P-value)
Age (y)	60.40±6.38	58.04±4.85	61.82±5.56	57.85±4.75	.129
Diabetic duration (y)	9.00±5.71	-	12.00±4.80	-	.050
High (m)	1.52±0.06	1.53±0.05	1.53±0.05	1.54±0.07	.052
Wight (Kg)	86.96±11.23	82.98±11.76	61.56±7.95	64.10±6.51	.000
BMI (Kg/m2)	37.60±4.65	35.25±4.72	26.19±2.03	27.16±1.97	.000
s-25-OH-D(nmol/L)	25.95±17.47	25.97±16.02	33.35±22.29	39.18±20.25	.062
s-iPTH(pmol/L)	8.81±4.16	8.58±4.08	8.47±3.13	8.04±3.28	.120
s-OC(ng/ml)	17.40±9.17	21.08±10±39	17.79±6.44	19.50±10.56	0.528
s-CTX(pg/ml)	283.40±180.41	358.79±197.49	319.10±192.99	346.80±213.86	0.499
s-Glucose (mmol/L)	8.77±2.77	4.90±0.45	9.15±3.47	4.73±0.44	.000
s-Insulin (uU/L)	19.36±12.67	11.65±5.58	11.29±7.23	9.22±6.21	.000
HOMA-IR	7.94±6.73	2.54±1.26	4.51±2.88	2.02±1.51	.000

Table 2 Shows the BMD values and T-score for spine, femur neck and total hip of Saudi women with and without diabetes. By using one-way ANOVA with bonferroni post hoc analysis to study differences between four subgroups of diabetic obese, diabetic overweight, diabetic obese and non-diabetic overweight and compared them to each other. Post hoc comparisons using the bonferroni test indicated that the BMD at lumbar spine was significantly lower in diabetic overweight (0.96±0.13 g/cm2) compared to diabetic obese (1.05±0.17 g/cm2) p = 0.05, and significantly lower in non-diabetic overweight (0.93±0.14 g/cm2) compared to diabetic obese (1.05±0.17 g/cm2) p = .013.

Table 2: Comparison between mean of BMD and T-score in diabetic and non-diabetic group

Variable	Diabetic obese	Non-diabetic obese	Diabetic overweight	Non-diabetic overweight	ANOVA (P-value)
Spine (L1-L4) BMD (g/cm2):	1.05±0.17	0.99±0.17	0.96±0.13	0.93±0.14	.058
T-score	-0.42±1.43	-0.88±1.46	-1.21±1.11	-1.28±1.23	0.091
Femur (neck) BMD (g/cm2):	0.90±0.15	0.88±0.11	0.84±0.12	0.83±0.09	0.479
T-score	-0.84±1.24	-0.56±0.98	-0.84±1.14	-0.96±0.84	0.652
Total hip BMD (g/cm2):	0.84±0.15	0.86±0.11	0.83±0.14	0.80±0.11	0.174
T-score	-0.33±1.29	-0.46±1.00	-0.85±0.95	-0.90±0.73	0.174

As a showed in figure 1 the correlation between vitamin D status and serum PTH in postmenopausal diabetic Saudi women. In diabetic obese, serum 25-OHD was significantly inversely correlated with PTH. In diabetic overweight and non-diabetic subgroup women there is negative correlation but no significant between serum 25-OHD and PTH.

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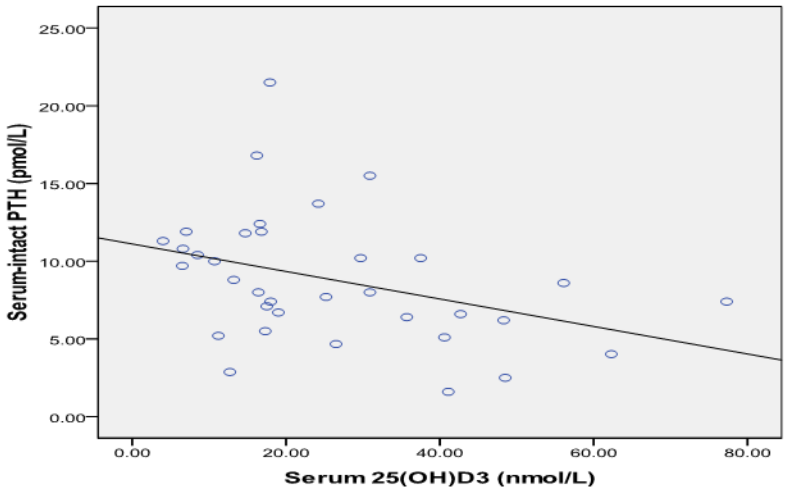

Figure 1: Correlation between serum 25-OH-D and PTH in diabetic obese women

The data were studied for association between BMI and bone mineral density at three skeletal sites, the lumbar spine, the total hip and the femur neck in postmenopausal women with T2DM and without T2DM. As shown in figure 2 (Pearson product-moment correlation) demonstrated that, there was a significant positive association in non-diabetic obese subgroup between BMI and BMD at lumbar spine.

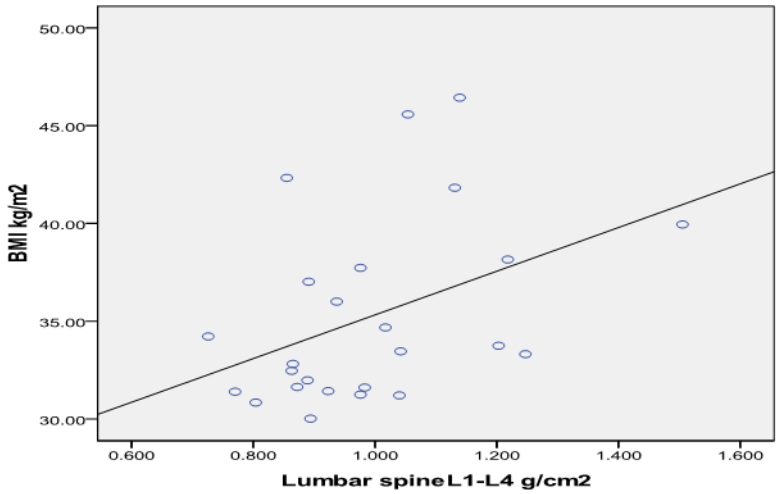

Figure 2: Correlation between lumbar spine and BMI for non-diabetic obese

The data were examined to correlated between 25-OHD and three sites of BMD, only significant positive correlation on non-diabetic obese at lumbar spine (Figure 3) while this data were examined to effect of 25-OHD on bone marker, OC and CTX, we found no correlated at OC and CTX with 25-OHD, except in overweight group we found negative correlated at OC (Figure 4). In non-diabetic overweight we observed negative significant at OC and CTX ($r = -.474$; $P< 0.05$ and $r = -0.638$; $P< 0.05$), (Figure 5) and (Figure 6) respectively.

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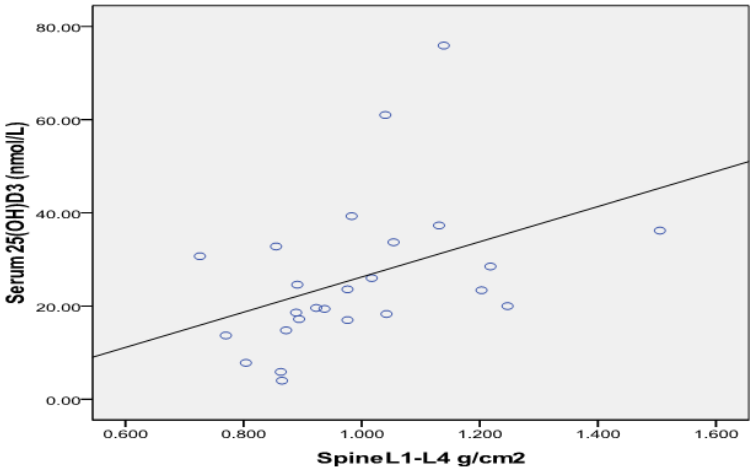

Figure 3: Correlation between 25-OHD and lumbar spine in non-diabetic obese

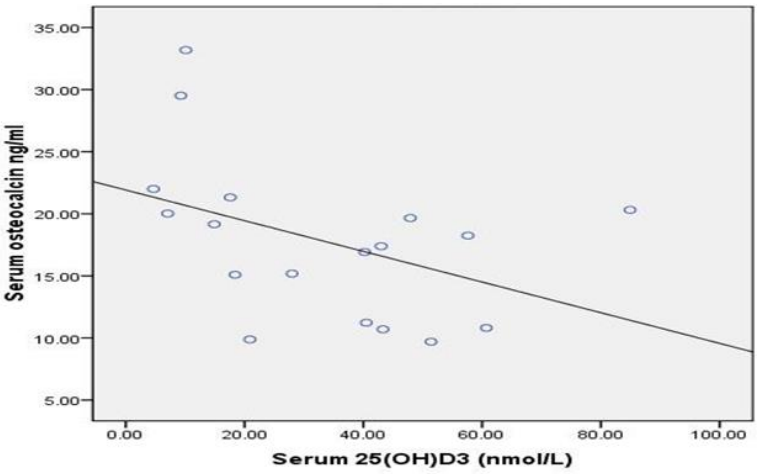

Figure 4: Correlation between 25-OH-D and OC in diabetic overweight

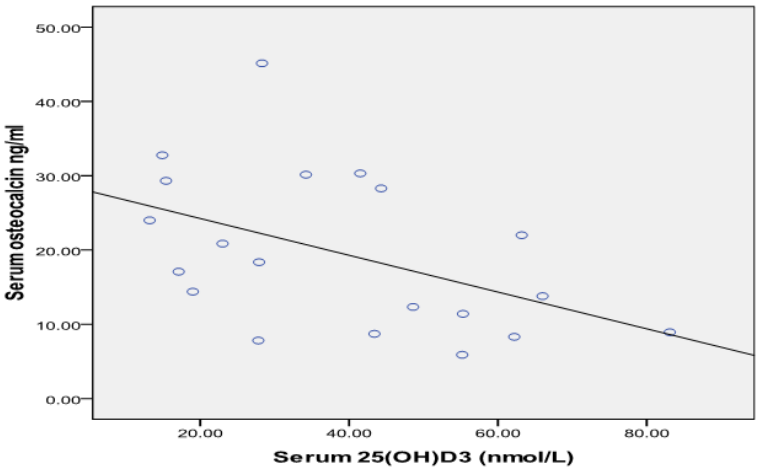

Figure 5: Correlation between 25-OH-D and OC in non-diabetic overweight

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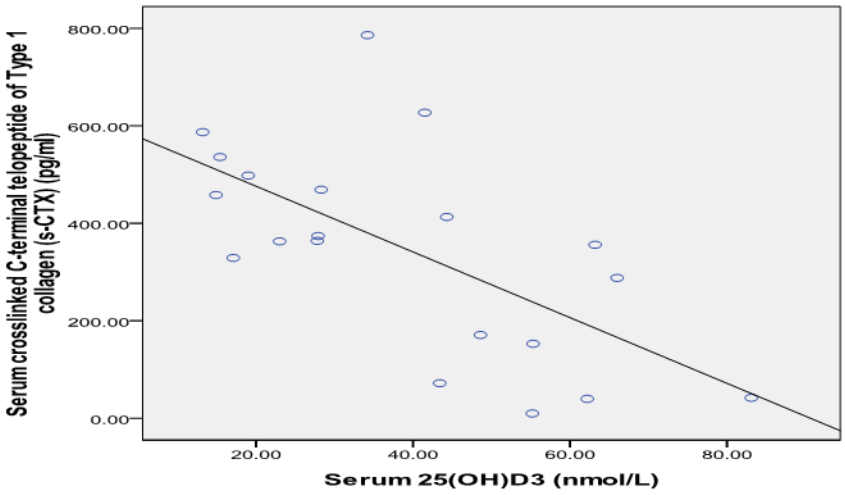

Figure 6: Correlation between 25-OH-D and CTX in non-diabetic overweight

DISCUSSION

In this study, we investigated the association between vitamin D, incidence of bone status and several factors affected to the bone integrity in Saudi postmenopausal women diagnosed with diabetes mellitus. (5, 6).

Vitamin D deficiency was 86 % and 81% respectively in diabetic and non-diabetic Saudi groups. It was inversely correlated to PTH in in diabetic obese women.

A low serum 25-OHD concentration is associated with a high risk of diabetes mellitus in Saudi women; levels of 25-OHD are low in obese group and are clearly associated with the degree of obesity. (1,7). Arrieta et al found in Obese class II; >40.0 (kg/m2) the level of 25OHD was lower in both T2DM and control group (8). Obesity is associated with reduced 25-OHD. Limited mobility and increased storage of vitamin D in fat tissue have been suggested as potential causes, but obesity is actually a consequence of low vitamin D levels (1,7,9).

A negative correlation between PTH and 25-OHD in diabetic obese subgroup (Fig.1) exhibited a significant inverse correlation agreeing with other studies (8,10,11).

In similar finding to previous study, we found no significant between 25-OHD and insulin sensitivity index, glucose, insulin, HOMA-IR and Hb1Ac in diabetic and non-diabetic subgroup (1). Recent studies suggest adequate vitamin D levels may be involved in decreasing insulin resistance, which is a contributing factor to the development of T2DM. (1,7). One study demonstrated that the lower level in serum of 25 OHD in diabetic groups because of increasing in fat mass. 12.

This study also showed a positive correlation between BMD at lumbar spine and 25-OHD in non-diabetic obese women (13) exhibited that increasing serum 25-OHD level related to higher BMD at all sites. Recent studies suggest that a low serum 25-OHD level is associated with low BMD (14,15, and 16).

Ma et al 2012 demonstrated that the BMD was higher in T2DM compared to healthy group control. Our data showed that at lumbar spine the result trend to be significant compared to control group (17).

In this presented study the BMI in postmenopausal Saudi women showed positive correlation between lumbar spine in diabetic obese (17). A study performed in China that BMI presented a positive correlation with bone incidence values as measured by DXA with diabetic overweight, and non-diabetic overweight, these results were in agreement with our study and those from previous studies on chines women that considered BMI (overweight and obese: BMI ≥ 25 kg/m2) (18,19).

Negative correlations were obtained between serum 25-OHD and bone formation markers serum OC in diabetic and non-diabetic overweight subgroup (Fig.4 and 5 respectively). Such results are carried out in Moroccan women and Saudi women among healthy postmenopausal women (14,20) and diabetic women (4,13). Also, negative correlations were evident between serum 25-OHD and bone resorption makers serum CTX among non-diabetic overweight subgroup (Fig.6) this result was supported by a previous study of healthy Saudi men (21, 22).

CONCLUSION

Since the most study subject considered as Vitamin D deficiency, non-exposure to sunlight, lack of exercise and negligible dairy food, it would be conclude that the low vitamin D can be attributed to diabetic mellitus and low BMD.

The diabetic women had a slightly higher mean BMD value than the non-diabetic. Our findings suggest that, bone formation and resorption are decreased in type 2 diabetes, this low bone turnover can slow bone loss rate and causes higher bone density than expected for their age and compared to non-diabetic groups. Nevertheless, the decrease in bone turnover level could also increase skeletal fragility.

Limitation

There are several limitations in this study. First, the sample size was not large enough. Secondly, Studies in subjects with T2DM frequently do not specify and/or analyze results on the basis of treatment type (diet vs. oral hypoglycemic agent vs. insulin), which could also account for the discrepancies in studies of bone density in T2DM.

In future study, very necessary to examine the effective the diabetic complications on BMDs. Diabetic complications like retinopathy, neuropathy, and angiopathy may influence the fracture event independently from bone mass

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DECLARATION OF INTEREST

The authors have declared no conflict of interest regarding this work

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