Plant Archives Volume 20 No. 2, 2020 pp. 4613-4620 **e-ISSN:2581-6063 (online), ISSN:0972-5210**

BONE MINERAL DENSITY AND VITAMIN D STATUS AMONG POSTMENOPAUSAL IRAQI WOMEN

Esraa Dawood Salman and Hind Shakir Ahmed*

Department of Chemistry, College of Education for Pure Science (Ibn Al-Haitham), University of Baghdad, Baghdad-Iraq.

Abstract

Menopause is the most prevalent cause of accelerated bone loss in women. Vitamin D insufficiency is predominant in postmenopausal women and has been related with low bone mineral density.

The present study intends to estimate the bone mineral density and the incidence of vitamin D3 deficiency among postmenopausal Iraqi women.

This study was carried through November 2019 to March 2020 at the Rheumatology and Rehabilitation Unit/ Baghdad Teaching Hospital- Medical City/ Baghdad, with a total of 35 postmenopausal women. Their ages ranged from 52-65 years and they were paralleled with 35 healthy premenopausal women as control group. All individuals were diagnosed by physicians in a Rheumatology and Rehabilitation Outpatient Clinic and the clinical data was collected along with the assessment of biochemical parameters.

There was a significant increase (p d" 0.05) in fasting serum glucose, total cholesterol, triacylglycerol, and low density lipoprotein cholesterol, whereas a significant decrease (p d" 0.05) in serum calcium and vitamin D3 were found in postmenopausal women as paralleled to premenopausal. Hypovitaminosis D were appeared in postmenopausal women (11.30±5.6 ng/ml) vs. 47.48±6.26 ng/ml in premenopausal. Also, there was a significant decrease (p= 0.0011) in bone mineral density and T-score in postmenopausal women as compared to premenopausal with OR and CI= 1.07 (0.76-1.52), 1.37 (0.87-1.76) receptively. Furthermore, there was a significant negative correlation between bone mineral density with body mass index and fasting serum glucose also between serum vitamin D3 and fasting serum glucose.

Hypovitaminosis D with low bone mineral density were associated with poor glycemic control and dyslipidemia among postmenopausal women.

***Key words*:** Postmenopause, Osteoporosis, Bone mineral density, Vitamin D3.

Introduction

The term natural menopause is defined as the perpetual termination of menstruation resulting from the defeat of ovarian follicular activity (WHO, 1996). The mean age at natural menopause is 51 years in developed country, while it is 48 years in poor and undeveloped country. This period brings several metabolic and hormonal changes reflecting a decrease in ovarian function (Sapre and Thakur, 2014).

Postmenopausal osteoporosis (PMOP) is a public metabolic bone disorder categorized by diminished bone mineral density (BMD) and raised fracture risks among postmenopausal women (Bandeira and Bilezikian, 2017).

Osteoporosis is a skeletal disorder manifested by reduced bone mass and deterioration of bone microarchitecture, leading to improved bone fragility and predisposition to fracture (Sugimoto *et al.*, 2016). Bone fragility is assessed by the micro-architectural quality which is determined by bone fracture, *i.e.* micro-architecture, micro-damage, and remodeling rate which affect the ability bone to resist fracture (Khamees *et al.*,

***Author for correspondence :** E-mail: hindshakir82@gmail.com

2018).

Bone remodeling is a lifelong process in vertebrates that relies on the balance between bone formation by osteoblasts and bone resorption by osteoclasts (Lv *et al.*, 2016). When the balance is disrupted, abnormal bone loss and osteoporotic fractures often occurs (Baum and Gravallese, 2014).

Various criteria for the diagnosis of osteoporosis have been recommended. Rendering to the World Health Organization (WHO), osteoporosis is defined as a BMD at the hip and/or the spine at least 2.5 standard deviations (SD) less the mean peak bone mass of young healthy adults as assessed by dual energy X-ray absorptiometry (DEXA) (WHO, 1994). On the other hand, BMD is affected by various factors like sex, genetics, and regional risk factors (Bartell *et al.*, 2011).

Calcium (Ca^{+2}) and vitamin D intake are associated with the BMD, and vary between osteoporotic and non-osteoporotic individuals (Hammad and Benajiba, 2017). Dietary patterns, high content foods of saturated fatty acids or low nutrients are unfavorable to bone health in menopausal women (Karamati *et al.*, 2012).

Vitamin D is a fat-soluble and vitamin D3 is obtained from the diet or through synthesis in the skin with the involvement of ultraviolet B radiation (UVB). For biological activity, it must first be hydroxylated in the liver to 25-hydroxyvitamin D (25(OH)D), which is the main circulating metabolite of vitamin D and reflects the amount of vitamin D in the body, and then in the kidneys to 1,25-dihydroxyvitamin D (1,25-$(OH)_2$-D), which its active form (Didriksen *et al.*, 2013). The reduced of vitamin D is detected in obese and overweight persons, which possibly results from the increased sequestration of this vitamin in adipose tissue. Vitamin D deficiency is closely related to visceral obesity. These hormonal changes lead to musculoskeletal, metabolic and cardiovascular (CV) complications and can disturb mental health, all of which being correlated with vitamin D deficiency (Pinkas *et al.*, 2017).

Thus, this work intends to estimate the BMD and the incidence of vitamin D3 deficiency among postmenopausal Iraqi women.

Materials and Methods

The present study was carried through November 2019 to March 2020 at the Rheumatology and Rehabilitation Unit/ Baghdad Teaching Hospital-Baghdad Medical City, with a total of 35 postmenopausal women; their ages ranged from 52-65 years. They were compared with 35 healthy premenopausal women as control group. The postmenopausal status was defined as termination of menses for at least 1 year. All individuals were examined and diagnosed by physicians in a Rheumatology and Rehabilitation Outpatient Clinic. Informed consent was taken from all cases prior to their enrollment in this study. A detailed history regarding menstrual history and duration of menopause are obtained. A social and medical history, features of osteoporosis including fragility fracture, intake of medications and supplements, personal history and family history of fractures, loss of height, bone pain and other complaints were elicited. Waist circumference (WC), systolic-, and diastolic blood pressure (SBP, DBP) were measured and body mass index (BMI) was calculated as weight in kilograms (Kg) divided by square of height in meters (m^2) (WHO, 2004). Osteoporotic women were diagnosed by DEXA. The diagnostic criteria of osteoporosis recommended by the WHO as shown in (Table 1). Resulting T-scores are used to interpret BMD and to associate results with fracture risk, *i.e.*, reduced BMD (or a greatly negative T-score) is associated with a great fracture risk.

Table 1: T scores and their indications in terms of BMD (WHO, 2004)

T-Score	Indication of BMD
e" -1	Normal
< -1 to > -2.5	Osteopenia
d" -2.5	Osteoporosis
d" -4	Sever osteoporosis

Biochemical Measurements

Laboratory assessments were down, which encompassed fasting serum glucose (FSG), total cholesterol (TC), triacylglycerol (TAG), high density lipoprotein cholesterol (HDL-C), low density lipoprotein cholesterol (LDL-C), very low density lipoprotein cholesterol (VLDL), serum Ca^{+2}, and alkaline phosphatase (ALP). All these tests were measured using a chemical analyzer. Serum vitamin D3 was estimated using mini VIDAS, BioMerieux kit, France. Hypovitaminosis is defined by most experts as a serum 25(OH)D level < 20 ng/ml, whereas a serum 25(OH)D level of > 30 ng/ml is deliberated to be normal and a level of 20–30 ng/ml describes vitamin D insufficiency (Holick, 2009).

Exclusion Criteria

Patients with diabetes, rheumatic disease, malignancy, liver, renal, or thyroid disorders were excepted. Also, individuals on treatments that might disturb bone metabolism as diuretics, ß-blockers, bisphosphonates, steroids, vitamin D or other anti-

osteoporotic medications were not included.

Statistical Analysis

All data are shown as means ± SD for all parameters. The *t*-test was used to equate experimental groups. Also, Odd ratio (OR), confidence interval (CI), and correlation coefficient (r) between variables were done in this study. A *p*-value d" 0.05 was deliberated statistically significant.

Results

Clinical and biochemical characteristics of menopausal women are shown in (Table 2). There was a significant increase (*p* d" 0.05) in age, WC, BMI, SBP, DBP, FSG, TC, TAG, LDL-C, VLDL, TC/HDL-C ratio, whereas significant decrease in serum HDL-C and Ca^{+2} were found in postmenopausal as paralleled to premenopausal women. Moreover, there was no significant difference in serum ALP between the two groups. The mean ± SD for duration of menopause was 9.50 ± 5.75 years.

Additionally, there was a significant reduction (*p*= 0.0001) in serum vitamin D3 level in postmenopausal women as paralleled to premenopausal women with OR= 1.59 and CI= 1.02-2.68. Also, there was a significant reduce (*p*= 0.0011) in BMD and T-score in postmenopausal women as compared to premenopausal with OR and CI= 1.07 (0.76-1.52), 1.37 (0.87-1.76) receptively, (Table 3).

Comparison of certain variables by vitamin D3 categorization is illustrated in (Table 4). There was a significant increase ($p < 0.05$) in BMI and FSG in postmenopausal women who had D3 deficient as compared to those with D3 insufficient.

Moreover, there was an increased in age, WC, SBP, DBP, serum TC, TAG, LDL-C, VLDL, TC/HDL-C ratio, ALP, and duration of menopause, while reduced in serum Ca^{+2}, BMD, and T-score were found in women who had deficient D3 as compared to those with insufficient.

Correlations regarding to D3 and BMD among postmenopausal women are shown in (Table 5). There was a significant negative correlation ($p < 0.05$) between serum vitamin D3 with SBP and FSG. While, there was no significant correlation between serum vitamin D3 and other parameters in table 5. Furthermore, a significant negative correlation ($p < 0.05$) was found between BMD with BMI and FSG. Whereas, a significant positive correlation (*p*= 0.0001) was detected between BMD and T-score among postmenopausal women and no statistically significant correlation between BMD and other parameters.

Table 2: Clinical and biochemical characteristics of menopausal women.

Parameters	Postmenopausal Women (n= 35)	Premenopausal Women (n= 35)	*p*-value
Age (Years)	59.25 ± 6.01	41.20 ± 5.51	0.001
WC (cm)	94.65 ± 9.18	74.65 ± 6.08	0.001
BMI (Kg/m^2)	28.11 ± 5.13	24.05 ± 1.23	0.05
SBP (mmHg)	134.8 ± 1.06	112.06 ± 0.77	0.0001
DBP (mmHg)	110.36 ± 8.26	77.50 ± 1.05	0.0001
FSG (mg/dl)	114.31 ± 10.44	97.74 ± 8.71	0.001
TC (mg/dl)	232.15 ± 12.96	137.90 ± 8.50	0.0001
TAG (mg/dl)	209.05 ± 8.75	102.97 ± 7.51	0.0001
HDL-C (mg/dl)	45.83 ± 10.31	55.77 ± 4.89	0.0449
LDL-C (mg/dl)	144.51 ± 8.45	61.63 ± 6.65	0.0001
VLDL (mg/dl)	41.81 ± 6.75	20.59 ± 5.90	0.0001
TC/HDL-C ratio	5.20 ± 1.93	2.47 ± 0.46	0.05
Ca^{+2} (mg/dl)	3.96 ± 1.22	9.81 ± 1.52	0.05
ALP (U/l)	67.25 ± 8.14	63.44 ± 7.26	0.232
Duration of Menopause (Years)	9.50 ± 5.75	-	-

Data are expressed as mean±SD. *p* d" 0.05: significant, WC: waist circumference, BMI: body mass index, SBP: systolic blood pressure, DBP: diastolic blood pressure, FSG: fasting serum glucose, TC: total cholesterol, TAG: triacylglycerol, HDL-C: high density lipoprotein cholesterol, LDL-C: low density lipoprotein cholesterol, VLDL: very low density lipoprotein, Ca^{+2}: calcium, ALP: alkaline phosphatase.

Discussion

One of the greatest significant alterations in the menopausal period

Table 3: Vitamin D3 level, BMD, and T-score in menopausal women

Parameters	Postmenopausal Women (n= 35)	Premenopausal Women (n= 35)	*p*-value	OR (CI)
Vitamin D3 (ng/ml)	11.30 ± 5.6	47.48 ± 6.26	0.0001	1.59 (1.02-2.68)
BMD (gm/cm^2)	0.772 ± 0.12	0.860 ± 0.09	0.0011	1.07 (0.76-1.52)
T-Score	-2.55 ± 1.03	-1.78 ± 0.79	0.0011	1.37 (0.87-1.76)

Data are expressed as mean±SD. *p* d" 0.05: significant, BMD: bone mineral density.

Table 4: Comparison of certain variables by vitamin D3 categorization

Variables	Postmenopausal Women (n= 35)		*p*-value
	Deficient D3< 20 ng/ml (n=25)	Insufficient D3 20-30 ng/ml (n=10)	
Age (Years)	59.67 ± 5.67	58.83 ± 8.44	0.255
WC (cm)	95.25 ± 8.50	94.05 ± 14.14	0.287
BMI (Kg/m^2)	30.89 ± 4.91	24.04 ± 1.24	0.05
SBP (Hg mm)	135.00 ± 1.15	132.80 ± 0.92	0.07
DBP (Hg mm)	112.25 ± 1.50	108.50 ± 0.77	0.06
FBS (mg/dl)	117.42 ± 10.27	110.25 ± 1.02	0.05
TC (mg/dl)	242.63 ± 11.04	221.67 ± 8.80	0.382
TAG (mg/dl)	209.84 ± 13.55	208.25 ± 15.38	0.966
HDL-C (mg/dl)	45.00 ± 5.03	46.67 ± 10.85	0.764
LDL-C (mg/dl)	155.67 ± 11.08	133.35 ± 6.61	0.440
VLDL (mg/dl)	41.96 ± 13.56	41.65 ± 17.37	0.966
TC/HDL-C ratio	5.39 ± 1.98	4.75 ± 1.67	0.578
Ca^{+2} (mg/dl)	3.99 ± 1.24	3.77 ± 1.19	0.743
ALP (U/l)	68.38 ± 14.08	66.12 ± 14.34	0.196
BMD (gm/cm^2)	0.752 ± 0.12	0.844 ± 0.10	0.221
T-Score	-2.75 ± 1.04	-1.98 ± 0.86	0.240
Duration of Menopause (Years)	10.51 ± 5.73	8.50 ± 6.27	0.418

Data are expressed as mean±SD. *p* d" 0.05: significant, WC: waist circumference, BMI: body mass index, SBP: systolic blood pressure, DBP: diastolic blood pressure, FSG: fasting serum glucose, TC: total cholesterol, TAG: triacylglycerol, HDL-C: high density lipoprotein cholesterol, LDL-C: low density lipoprotein cholesterol, VLDL: very low density lipoprotein, Ca^{+2}: calcium, ALP: alkaline phosphatase, BMD: bone mineral density.

Table 5: Correlations according to D3 and BMD in postmenopausal group

Variables	Vitamin D3 (ng/ml)		BMD (gm/cm^2)	
	r	*p*	r	*p*
Age (Years)	0.14	0.407	-0.04	0.787
WC (cm)	-0.13	0.453	-0.04	0.801
BMI (Kg/m^2)	-0.26	0.125	-0.34	0.043
SBP (Hg mm)	-0.38	0.021	-0.05	0.761
DBP (Hg mm)	0.47	0.0044	0.04	0.788
FSG (mg/dl)	-0.98	0.0001	-0.75	0.001
TC (mg/dl)	-0.003	0.983	0.07	0.657
TAG (mg/dl)	-0.01	0.938	0.09	0.596
HDL-C (mg/dl)	0.02	0.882	0.01	0.923
LDL-C (mg/dl)	-0.002	0.991	0.006	0.969
VLDL (mg/dl)	-0.01	0.938	0.09	0.596
TC/HDL-C ratio	-0.001	0.994	0.07	0.691
Ca^{+2} (mg/dl)	0.07	0.661	0.01	0.935
ALP (U/l)	0.24	0.157	0.009	0.958
T-Score	0.29	0.081	0.99	0.0001
Duration of Menopause (Years)	0.15	0.382	0.14	0.417

p d" 0.05: significant, WC: waist circumference, BMI: body mass index, SBP: systolic blood pressure, DBP: diastolic blood pressure, FSG: fasting serum glucose, TC: total cholesterol, TAG: triacylglycerol, HDL-C: high density lipoprotein cholesterol, LDL-C: low density lipoprotein cholesterol, VLDL: very low density lipoprotein, Ca^{+2}: calcium, ALP: alkaline phosphatase, BMD: bone mineral density.

denotes to the alterations in body composition factors principally due to hormonal changes through this period (Banack *et al.*, 2018). The mean ± SD for age at menopause in this study was 59.25 ± 6.01 years, which is in a harmony with prior study (Schoenaker *et al.*, 2014). Moreover, significant changes have been observed in postmenopausal women as in WC and BMI. This may be due to the complex relationship between BMI and hypothalamus-pituitary gland axis functions. Similar observation was reported previously (Ahmed, 2017a).

Postmenopausal women are also documented to reveal greater fat percentage, total body fat mass, and accumulation of central fat than premenopausal women (Razmjou *et al.*, 2018). Kim et al, postulated that although both pre- and post-menopausal women had parallel mean BMI values, but postmenopausal women had larger WC (Kim *et al.*, 2007).

Aging is related with variations in body composition, which disturb physical activity and humans health (Russell and Grossmann, 2018). Primary osteoporosis is often related with age and sex hormone insufficiency. Age-associated osteoporosis results from the continuous worsening of the trabecular in bone. Additionally, the decrease production of estrogen among postmenopausal women leads a significant increase in bone loss, which may contribute to the decrease in BMD with time (Tu *et al.*, 2015). It has documented that endogenous sex hormones can disturb the lipid profile in postmenopausal women because the androgen and estrogen receptors are expressed in visceral and subcutaneous adipocytes. Consequently, alterations in the endogenous sex hormones concentrations may disturb lipid metabolism in the fat tissues among middle-aged women (Marchand *et al.*, 2018).

Menopause-induced estrogen diminished may also lead to several metabolic disturbance, comprising lipid metabolism defect (Ko and Kim, 2020). In this study, all menopausal women had lipid abnormalities.

Metabolic and hormonal alterations in postmenopausal women are related with greater body weight and visceral fat accumulation, which leads to the occurrence of high abdominal obesity. As revealed formerly, TC, TAG, LDL-C, HDL-C and TC/HDL-C ratio are generally changed in postmenopausal women with a 50% risk of having metabolic disorders (Ebtekar *et al.*, 2018). The lipids ratios predict CV risk better than isolated lipoprotein sub-fractions. This study showed there was a significant raised (p=0.001) in TC/HDL-C ratio in cases as paralleled to healthy, which is in accordance with prior study (Ahmed, 2017b).

Menopause is also, a risk influence that is accompanied with an imbalance in bone metabolism. Around 35% of postmenopausal women has low BMD are at improved risk of osteoporosis and suffering of fractures over the years (Lanzillotti *et al.*, 2003). Although 90% of BMD is genetically determined, a greater peak BMD can be simplified by confirming modifiable influences are optimized, comprising nutrition, exercise and other lifestyle influences. The diminish in estrogen production is the chief element of this imbalance, concurring with a decreased level of Ca^{+2} absorbed by the intestine, due to the low production of calcitonin, a hormone that suppress bone demineralization, though many other influences may donate (Blackie, 2020).

Fat and bone are linked by many pathways providing a skeleton suitable to the mass of adipose tissue it is carrying. However, increased body fat, and predominantly abdominal fat, causes production of inflammatory cytokines which may consequently activate bone resorption, resulting in reduction of bone strength (Sakhaee *et al.*, 2016).

Under normal physiological situations, mechanical loading show a main role in attaining bone mass, bone strength, and bone size. Previous data from osteoporosis study, a subgroup of the whole study, revealed the strong influence of weight on BMD, proposing that this influence is due to mechanical loading on weight bearing axes (Zhao *et al.*, 2007). Obesity was believed to be defensive against PMOP, because obese women had greater BMD. Then, it has revealed that accumulative fat mass may not have a favorable influence on bone mass (Hollick *et al.*, 2002).

In the current study, there was a decrease in serum Ca^{+2} level in PMOP patients as paralleled to the controls, which is in accordance with previous data (Ahmed, 2017c). Also, there was a significant difference between the levels of serum Ca^{+2} and vitamin D3 in post- and pre-menopausal women, which rendering the occurrence of osteoporosis with or without vertebral fracture, because bone formation markers are constituents secreted by osteoblasts through osteoblast differentiation. These outcome indicate that osteoporotic patients encompassed in this study didn't have metabolic bone disease other than osteoporosis. Parallel outcomes have been described by Delmas et al, which showed that the normal levels of serum ALP in osteoporotic cases reflect different phases of osteoblast in bone formation (Delmas *et al.*, 2000).

Genetic, physiological, environmental, and modifiable lifestyle factors can also play a significant role in bone mass. Vitamin D has a varied range of biological roles,

comprising Ca^{+2} and phosphate homeostasis, skeletal metabolism, and vascular function by increasing Ca^{+2} absorption in the intestines, stimulating bone resorption by increasing number of osteoclasts, and maintain level of parathyroid hormone (PTH) to stabilize serum Ca^{+2} levels (Zhao *et al.*, 2016). Hypovitaminosis D is a significant risk factor for the progress of osteoporosis. In the present study, 25 women of postmenopausal group had deficiency in vitamin D3 (< 20 ng/ml) and 10 had insufficiency.

A vitamin D deficiency leads to a lessening in the intestinal absorption of Ca^{+2}, decreasing its status and causing the release of PTH levels of which are contrary proportionate to the levels of 25(OH)D (Ferreira *et al.*, 2015). In menopause period, women will have thinner skin and a lesser capacity for vitamin D production, in addition to a reduction of intestinal absorption of vitamin D and hydroxylation of vitamin D in the liver and kidneys. These metabolic disorders will be attended by a tendency towards limited outdoor activity and a lesser dietary intake of vitamin D (Alissa *et al.*, 2014).

Hypovitaminosis D might have an influence on insulin secretion. Probably, the increased intracellular Ca+2 dephosphorylates glycogen synthase and impairs glucose transporter (GLUT-4). This continually increased Ca+2 level inhibits the cells from sensing Ca+2 fluxes essential for insulin associated actions. These Ca+2 fluxes are also essential for the ß-cells to secrete insulin (Girgis *et al.*, 2014).

In the current study, the BMD T-score had no association with vitamin D3 concentrations in correlation statistics in postmenopausal women. Vitamin D levels represent the current vitamin D status of an individual, while BMD T-score denotes bone mineral accrual over a period of time depending upon a diversity of other influences, which is in accordance with prior data (Kamineni *et al.*, 2016). Additionally, Shenoy et al, who found that low vitamin D3 status was significantly associated with atherogenic lipid profile in euglycemic subjects (Shenoy *et al.*, 2014).

Studies from different Arabian and European countries recommended that vitamin D supplement treatment could advance glycemic control (Bogdanou *et al.*, 2017; Hafez *et al.*, 2017).

It has recommended that vitamin D3 can modify the lipid profile by direct and indirect mechanisms. It can directly decrease TAG levels by increasing the activity of lipoprotein lipase in adiposity (Wang *et al.*, 2009). It can also indirectly reduce the serum levels of TC and LDL-C as Ca+2 interferes with fatty acid absorption through the formation of insoluble Ca+2-fatty complexes in the gut, resulting in increasing the conversion of cholesterol to bile acids (Christensen *et al.*, 2009).

Conclusions

Hypovitaminosis D with low BMD were associated with poor glycemic control and dyslipidemia among postmenopausal women, which mean that early detection of vitamin D deficiency and supplementation may help in the improvement of glycemic control and prevent of dyslipidemia. Thus, osteoporosis is predominant among postmenopausal Iraqi women concerning the occurrence of osteoporotic fractures in those women and hence, absence of strategies for prevention and management were observed. Preventive measures against osteoporosis should be considered to improve bone health.

Acknowledgements

Special thanks to all the healthy subjects and patients who approved to contribute in the current study and sincere thanks to the Rheumatology and Rehabilitation Unit/ Baghdad Teaching Hospital/ Baghdad Medical City.

References

Ahmed, H.S. (2017a). Metabolic and hormonal changes associated with menopause. *Mustansiriya Medical Journal*, **16(3)**: 77-82.

Ahmed, H.S. (2017b). A comparative estimation of metabolic and hormonal parameters among Iraqi hypothyroid patients. *The Iraqi postgraduate medical journal*. **16(2)**: 204-9.

Ahmed, H.S. (2017c). Correlations between serum interleukins-2,-4 levels and some biochemical parameters in Iraqi patients with osteoporosis. *Fac Med Baghdad*, **59(3)**: 275-9.

Alissa, E.M., W.A. Alnahdi, N. Alama and G.A. Ferns (2014). Serum osteocalcin is associated with dietary vitamin D, body weight and serum magnesium in postmenopausal women with and without significant coronary artery disease. *Asia. Pac. J. Clin. Nutr*. **23(2)**: 246–55.

Banack, H.R., J. Wactawski-Wende, K.M. Hovey and A. Stokes (2018). Is BMI a valid measure of obesity in postmenopausal women? *Menopause*, **25(3)**: 307–13.

Bandeira, L. and J.P. Bilezikian (2017). Novel Therapies for Postmenopausal Osteoporosis. *Endocrinology and metabolism clinics of North America*. **46(1)**: 207–219.

Bartell, S.M., S. Rayalam, S. Ambati, D.R. Gaddam, D.L. Hartzell, M. Hamrick, J.X. She, M.A. Della-Fera and C.A. Baile (2011). Central (ICV) leptin injection increases bone formation, bone mineral density, muscle mass, serum IGF-1, and the expression of osteogenic genes in leptin-deficient ob/ob mice. *J Bone Min Res*. **26(8)**: 1710-20.

Baum, R. and E.M. Gravallese (2014). Impact of inflammation

on the osteoblast in rheumatic diseases. *Curr. Osteoporos. Rep*. **12(1)**: 9–16.

Blackie, R. (2020). Diagnosis, assessment and management of osteoporosis. *Prescriber*, **31(1)**: 14-9.

Bogdanou, D., M. Penna-Martinez, N. Filmann, T.L. Chung, Y. Moran-Auth, J. Wehrle, C. Cappel, S. Huenecke, E. Herrmann, U. Koehl and K. Badenhoop (2017). T-lymphocyte and glycemic status after vitamin D treatment in type 1 diabetes: A randomized controlled trial with sequential crossover. *Diabetes Metab Res Rev*. **33(3)**.

Christensen, R., J.K. Lorenzen, C.R. Svith, E. Bartels, E. Melanson, W. Saris, A. Tremblay and A. Astrup (2009). Effect of calcium from dairy and dietary supplements on faecal fat excretion: a meta-analysis of randomized controlled trials. *Obes Rev*. **10(4)**: 475–86.

Delmas, P.D., R. Eastell, P. Garnero, M.J. Seibel, J. Stepan and Committee of Scientific Advisors of the International Osteoporosis Foundation (2000). The use of biochemical markers of bone turnover in osteoporosis, *OsteoporosInt* **11(6)**: S2–S17.

Didriksen, A., G. Grimnes, M.S. Hutchinson, M. Kjærgaard, J. Svartberg, R.M. Joakimsen and R. Jorde (2013). The serum 25-hydroxyvitamin D response to vitamin D supplementation is related to genetic factors, BMI, and baseline levels. *Eur. J. Endocrinol*. **169(5)**: 559–67.

Ebtekar, F., S. Dalvand and R.G. Gheshlagh (2018). The prevalence of metabolic syndrome in postmenopausal women: A systematic review and meta-analysis in Iran. *Diabetes Metab. Syndr*. **12(6)**: 955–60.

Ferreira, D.F., T.M. Rocha, Klein M.R.S.T. and A.F. Sanjuliani (2015). Vitamin d deficiency is associated with insulin resistance independent of intracellular calcium, dietary calcium and serum levels of parathormone, calcitriol and calcium in premenopausal women. *Nutr. Hosp.*, **31(4)**:1491–98.

Girgis, C.M., N.K.M. Cha, P.J. Houweling, M. Abboud, D.R. Fraser, R.S. Mason, R.J. Clifton-Bligh and J.E. Gunton (2014). The vitamin D receptor (VDR) is expressed in skeletal muscle of male mice and modulates 25-hydroxyvitamin D (25OHD) uptake in myofibers. *Endocrinology*, **155(9)**: 3227–37.

Hafez, M., M. Hassan, N. Musa, S. Abdel Atty and S.A. Azim (2017). Vitamin D status in Egyptian children with type 1 diabetes and the role of vitamin D replacement in glycemic control. *J Pediatr Endocrinol Metab*. **30(4)**: 389-94.

Hammad, L.F. and N. Benajiba (2017). Lifestyle factors influencing bone health in young adult women in Saudi Arabia. *Afr. Health. Sci*. **17(2)**: 524–31.

Holick, M.F. (2009). Vitamin D status: Measurement, interpretation, and clinical application. *Ann Epidemiol*. **19(2)**: 73 8.

Hollick, M.F. (2002). Vitamin D: the underappreciated D-lightful hormone that is important for skeletal and cellular health. *Curr Opin Endocr Diab*. **9**: 87-98.

Kamineni, V., A.P. Latha and K. Ramathulasi (2016). Association between serum 25-hydroxyvitamin D levels and bone mineral density in normal postmenopausal women. *J. Mid-life Health*, **7(4)**: 163-8.

Karamati, M., M. Jessri, S.E. Shariati-Bafghi and B. Rashidkhani (2012). Dietary patterns in relation to bone mineral density among menopausal Iranian women. *Calcif. Tissue. Int.*, **91(1)**: 40-9.

Khamees, A.H., A.J. Abdulhussein, H.B. Sahib and H.A. Fawzi (2018). Anti-angiogenic and antioxidant activity of Iraqi cyperus rotundus ethanol extract. *Int. J. Pharmacol*., **14(4)**: 546-52.

Kim, H.M., J. Park, S.Y. Ryu and J. Kim (2007). The effect of menopause on the metabolic syndrome among Korean women: The Korean National Health and Nutrition Examination Survey, 2001. *Diabetes Care*, **30(3)**: 701–6.

Ko, S. and H. Kim (2020). Menopause-associated lipid metabolic disorders and foods beneficial for postmenopausal women. *Nutrients*, **12(1)**: 1-25.

Lanzillotti, H.S., R.S. Lanzillotti, A.P.R. Trotte, A.S. Dias, B. Bornand and E.A.M.M. Costa (2003). Osteoporose em mulheres na pós-menopausa,cálcio dietético e outros fatores de risco. *Rev Nutr*., **16(2)**: 181–93.

Lv L., Ge Wenshu, Liu Yunsong, Lai Guanyou, Liu Hao, Li Wenyue and Zhou Yongsheng (2016). Lysine-specific demethylase 1 inhibitor rescues the osteogenic ability of mesenchymal stem cells under osteoporotic conditions by modulating h3k4 methylation. *Bone Res*., **4(37)**: 16037.

Marchand, G.B., A.M. Carreau, S.J. Weisnagel, J. Bergeron, F. Labrie, S. Lemieux and A. Tchernof (2018). Increased body fat mass explains the positive association between circulating estradiol and insulin resistance in postmenopausal women. *Am. J. Physiol. Endocrinol. Metab*., **314(5)**: E448–E56.

Pinkas, J., I. Bojar, M. Gujski, J. Bartosinska, A. Owoc and D. Raczkiewicz (2017) Serum Lipid, Vitamin D Levels, and Obesity in Perimenopausal and Postmenopausal Women in Non-Manual Employment. *Med. Sci. Monit*., **23**: 5018–26.

Razmjou, S., J. Abdulnour, J.P. Bastard, S. Fellahi, E. Doucet, M. Brochu, J.M. Lavoie, R. Rabasa-Lhoret and D. Prud'homme (2018). Body composition, cardiometabolic risk factors, physical activity, and inflammatory markers in premenopausal women after a 10-year follow-up: A MONET study. *Menopause*, **25(1)**: 89–97.

Russell, N. and M. Grossmann (2018). Management of bone and metabolic effects of androgen deprivation ngfldsturr4sdb dtherapy. Urol. Oncol. S1078-1439(18), 30389-2.

Sakhaee, K., J. Poindexter and C. Aguirre (2016). The effects of bariatric surgery on bone and nephrolithiasis. *Bone*, **84**:1–8.

Sapre, S. and R. Thakur (2014). Lifestyle and dietary factors determine age at natural menopause. *J Midlife Health*, **5(1)**: 3-5.

Schoenaker, D.A., C.A. Jackson, J.V. Rowlands and G.D. Mishra (2014). Socioeconomic position, lifestyle factors and age at natural menopause: a systematic review and metaanalyses of studies across six continents. *Int. J. Epidemiol*, **43(5)**: 1542-62.

Shenoy, V., P. Datta, K. Prabhu and K. Singh (2014). Association between vitamin D, fasting blood glucose, HbA1c and fasting lipid profile in euglycemic individuals. *J Res Diabetes*, **2014(929743)**: 1-8.

Sugimoto, T., M. Sato, F.C. Dehle, J.M. Alan, M.S. Brnabic, Weston and R. Burge (2016). Lifestyle-Related Metabolic Disorders, Osteoporosis, and Fracture Risk in Asia: A Systematic Review. Value in health regional issues 9C, 49–56.

Tu, K.N., J.D. Lie, C.K. Wan, M. Cameron, A.G. Austel, J.K. Nguyen, K. Van and D. Hyun (2018). Osteoporosis: A review of treatment options. *P. and T.*, **43(2)**: 92-104.

Wang, J.H., T. Keisala, T. Solakivi, A. Minasyan, A.V. Kalueff and P. Tuohimaa (2009). Serum cholesterol and expression of Apo A? , LXR ß and SREBP2 in vitamin D receptor knock-out mice. *J Steroid Biochem Mol Biol*., **113(3-5)**: 222–6.

World Health Organization. (WHO). Scientific Group on Research on the Menopause in the 1990s (1994: Geneva, Switzerland) & World Health Organization (1996) Research on the menopause in the 1990s : report of a WHO scientific group. World Health Organization. 866, 107.

World Health Organization. WHO scientific group on the assessment of osteoporosis at primary health care level (2004). Summary Meeting Report. Brussels, Belgium: World Health Organization.

Zhao, L.J., Y.J. Liu, P.Y. Liu, J. Hamilton, R.R. Recker and H.W. Deng (2007). Relationship of obesity with osteoporosis. *J. Clin. Endocrinol Metab*., **92(5)**: 1640–6.

Zhao, B., W. Zhang, S. Du and Z. Zhou (2016). Vitamin D receptor BsmI polymorphism and osteoporosis risk in post-menopausal women. *Archives of medical science: AMS* **12(1)**: 25-30.