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Research Article

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Associations Factors Affecting on Osteoporosis in Postmenopausal Women in Saudi Arabian, Jeddah

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ABSTRACT

Background: *Osteoporosis is a disorders having the characteristic features of low Bone Mineral Density (BMD). However; there are several factors affecting the prevalence of osteoporosis in postmenopausal women as age, menopause, anthropometric measurements and biochemical bone markers.*
Objective: *This study aims to assess whether there is an association between age, anthropometric measurements, some serum biochemical bone indices (vitamin D, calcium, intact PTH, and magnesium) and bone health. Furthermore, we examine the axial and peripheral BMD.*
Design: *A cross-sectional study, involving 200 woman (50-82 years), it conducted in Jeddah, Saudi Arabia, during the year 2015. Anthropometric measurements for each participants were recorded. Calcium, vitamin D, intact PTH, magnesium, alkaline phosphates and cholesterol levels were measured. Lumbar spine (L1L4)), neck (NK), wards (WA), troch (Tr) and total femur (TF) BMD were performed in women by Dual-energy x-ray absorptiometry (DXA).*
Results: *Women age was 58.83 ± 5.89 Y, with menopausal age 51.38 ± 3.44 Y. Body Mass Index (BMI) of participants was 31.48 ± 5.68 kg/m2. The serum calcium, magnesium and alkaline phosphates were in normal range reached (2.54± 0.21 mmol/L, 0.79± 0.08 mmol/L and 1.34± 0.17 mmol/L, respectively). Most of participants suffering from deficiency of vitamin D and hyperparathyroidism reached (35.01 ± 22.08 nmol/L and 8.86 ± 3.28 pmol/L, respectively). as well as most of them have cholesterol level < 5.2 mmol/L. There was positive significant correlation between age and wait/hip ratio (0.18, p < 0.01). All BMD measure results, revealed negative significant correlation (p<0.001) with age recorded (- 0.31, -0.36, -0.39 and -0.40 for L1L4, NK, WA and TF, respectively), except Tr revealed showed positive significant correlation (0.33, p<0.001). As well as, BMD at the five sites measure revealed positive significant correlation (p<0.001) with body mass index (BMI). Also, negative significant correlation between PTH and vitamin D (0.18, p < 0.01) was found.*
Conclusion: *To prevent osteoporosis the postmenopausal women should have adequate intake of calcium and vitamin D in early ages. Proper nutrition education program should be done, especially during menopause transition and period for increase bone loss.*

Key words: *Postmenopausal women, Cross-sectional study, Associations factors, Saudi Arabian*

INTRODUCTION

Osteoporosis continues to be a prominent concern in women's health. Osteoporotic patients have decline Bone Mineral Density (BMD) and structural deterioration of bone tissues [1]. Numerous therapies and public health recommendations have been made to prevent and cure this disease. Bone loss occurs naturally with age, however; several factors contribute to the "un-coupling" of bone resorption, formation and accelerating losses in bone tissue. It has been estimated that 34% of healthy Saudi women with age of 50-79 years are osteoporotic [1-2]. Both BMD

and bone metabolism determine risk for osteoporosis or osteopenia, they can be effected by genetic, and nutritional factors [2].

One of the most importance nutrients to be considered to bone health is calcium. However, a regular diet is inadequate in calcium nutrient. On the other hand, vitamin D may potentially prevent the metabolic bone disorders, and musculoskeletal/mineral diseases [3]. Parathyroid hormone is the most important regulator of bone resorption and bone mass, it increases in response to depleted calcium and vitamin D concentrations [4]. Strong correlation between calcium and vitamin D concentrations, to serum PTH levels and femoral neck BMD was found [5]. Serum 25-hydroxyvitamin D level was inversely associated with serum PTH concentration independent of calcium intake [6]. Magnesium is the fourth most abundant mineral in the body, and it naturally found in many foods, and available as a dietary supplement [7]. It plays several important roles in decreasing the risk of neuromuscular disorders, cardiac arrhythmias, disordered bone metabolism and lowering osteoporosis [8].

A large number of etiological factors may lead to a reduce BMD, but the most common form of osteoporosis is seen in postmenopausal in which the estrogen deficiency is a major risk factor in early and the late phase of bone loss in women, since estrogens have a very favorable, antiresorptive and a discreet anabolic effect on bone tissue [9]. It has an important role in osteoblasts and mineral homeostasis [10]. In women the loss of bone mass increases several years after menopause, and the possibility of fractures increase in postmenopausal women while in men bone mass loss occurs slowly.

Therefore, this study examined the association between the serum calcium, magnesium, vitamin D, PTH, and bone health. As well as examined this finding further by considering axial and peripheral bone mass and markers of bone metabolism.

Subjects and Methods:

Selection of subjects

Cross-sectional study was used, this study was done during the year 2015. The including criteria was postmenopausal women 50 years or more, who had their last menstrual period at least one year and follicular stimulating hormone (FSH) level > 15 mIU/L[11]. As well as who with no chronic diseases as diabetics, hypertension, who not receiving drugs effect on bone metabolism. After applied the criteria 200 postmenopausal women (50-82 years) were included in this study.

After providing written informed consent, medically examination was done for all participants. The required information was collected by standardized questionnaire applied through personally interviewed. Anthropometric measurement; body weight and height with calculated BMI, and waist-to-hip ratio (WHR) were recorded.

Blood collection

Blood samples were collected from venous at 8:30 and 11 am under standardized conditions, after 12 hrs fasting. The serum was separated then stored -80ºC until used for determination of calcium, vitamin D, PTH, magnesium, alkaline phosphates and cholesterol level. The following reference ranges were used from King Abdulaziz University hospital lab for serum level of calcium (2.2-2.6 mmol/L), vitamin D (51-75 nmol/L), PHT (1.6 -6.9 pmol/L), magnesium (0.65-1.05 mmol/L) and for alkaline phosphates (50-136 mmol/L) and for cholesterol < 5.2 mmol/L.

Bone mineral density

Lumbar spine, neck, wards, troch and total femur bone mineral density was performed in all women, using Dual-energy x-ray absorptiometry (DXA) belongs to Center of Excellence for Osteoporosis Research (CEOR), King Abdulaziz University, Jeddah, Saudi Arabia,

Statistical analysis

Statistical analyses of data were carried out using SPSS version 22. Data were expressed as the mean ± SD. Association between variables was examined by Pearson's correlation coefficient. Differences were considered significant if $p < 0.05$.

RESULTS

Demographic and anthropometric data of postmenopausal women

General characteristics and anthropometric variables of postmenopausal women participants are described in Table (1). The mean age for the women in this study was 58.83± 5.89 Y with range (50-82 Y). Age at menarche was 12.81±1.59 Y with range (9-17 Y), while the age of menopausal was 51.38 ± 3.44 Y with range (42-61 Y). The number of pregnancies was about 6 times, number of kids born alive was 5 as median, and mean lactation in months was 9.39 ± 7.19. Regarding the anthropometric data the obtained results revealed that the mean height was 1.54 ± 0.59 (m) , weight was 74.76 ± 13.98 kg with body mass index 31.48 ± 5.68 kg/m2. Concerning waist circumference was 90.87 ± 11.82 cm, hip circumference106.42 ± 11.76 cm with waist to hip ratio 0.86 ± 0.84 cm^2

TABLE 1: Postmenopausal demographic characteristics and anthropometric data

Age (Y)	58.83± 5.89 (50-82; 58.00)
Menarche age (Y)	12.81±1.59 (9-17; 13.00)
Number of pregnancies	6.19± 3.37 (0-20; 6.00)
Number of kids born alive	4.99±2.62 (0-14; 5.00)
Lactation in months	9.39 ± 7.19 (0-24; 8.00)
Age at menopausal (Y)	51.38 ± 3.44 (42-61; 51.00)
Height (m)	1.54 ± 0.59 (1.39-1.69; 1.54)
Wt (Kg)	74.76 ± 13.98 (38-115; 73.00)
BMI (Kg/m^2)	31.48 ± 5.68 (17.83- 54.49; 31.16)
WC(Cm)	90.87 ± 11.82 (58-124; 90.00)
HC (Cm)	106.42 ± 11.76 (79-166; 106.00)
W/H ratio (Cm^2)	0.86 ± 0.84 (0.53- 1.22; 0.85)

Mean ± SD; range and median. N=200.

Biomarkers indices of bone metabolism

Some serum biochemical bone indices in postmenopausal women participated in this study was illustrated in Table (2). The results showed that the mean serum level of calcium recorded 2.54 ± 0.21 mmol/L which within reference value. Vitamin D 35.01 ± 22.08 nmol/L, thus indicated that the participants suffering from insufficiency/deficiency of vitamin D. Most of participants suffering from hyperparathyroidism, where the mean level of PTH was 8.86±3.28 pmol/L. Both magnesium (0.79± 0.08 mmol/L) and alkaline phosphates (1.34± 0.17 mmol/L) were in normal range for the participants. While cholesterol level is above the accepted value for the same age and gender for selected women it reached (5.75 ± 0.92 mmol/L).

TABLE 2: Some serum biochemical bone indices in postmenopausal women

Calcium (mmol/L)	2.54± 0.21 (2.17-2.99; 2.50)
Vitamin D (nmol/L)	35.01 ± 22.08 (4.00-140.00; 29.00)
Parathyroid hormone (PTH) (pmol/L)	8.86±3.28 (2.5-20.2; 8.40)
Magnesium (mmol/L)	0.79± 0.08 (0.50-1.00; 0.80)
Alkaline Phosphates (mmol/L)	1.34± 0.17 (0.76-1.94; 1.32)
Cholesterol (mmol/L)	5.75 ± 0.92 (3.90-8.50; 5.70)

Mean ± SD; range and median., N=200.

Bone mineral density

According to the obtained results from DXA for the study women in Table (3), it found that the mean BMD for lumbar spine L1L4, neck, wards, troch, total femur was 0.99 ± 0.15, 0.85 ± 0.13, 0.65 ± 0.35, 0.68 ± 0.12 and 0.87 ± 0.13 g/cm^2, respectively.

TABLE 3: Lumbar spine, neck, wards, troch and total femur BMD (g/cm2)in postmenopausal women

Lumbar spine L1L4	0.99± 0.15 (0.56-1.56; 0.97)
Neck	0.85 ± 0.13 (0.52- 1.26; 0.82)
Wards	0.65 ± 0.35 (0.35- 1.16; 0.64)
Troch	0.68 ± 0.12 (0.37- 1.08; 0.68)
Total femur	0.87 ± 0.13 (0.53- 1.35; 0.86)

Mean ± SD; range and median.

Matrix Pearson correlation

Table 4 shows Pearson correlation coefficients (r) between anthropometric data, age of menarche, some biomarkers indices of bone metabolism and bone mineral density. The obtained results revealed that, there was negative significant correlation between age and Ht (- 0.23, $p<0.01$), Wt (-0.15, $p<0.05$), HC(-0.15), with positive significant correlation with W/H(0.18, $p<0.01$). All DXA results revealed negative significant ($p<0.001$) correlation with age recorded -0.31, -0.36, -0.39 and -0.40 for L1L4, NK, WA and TF, except Tr revealed positive significant ($p<0.001$) correlation (0.33). Positive significant ($p<0.001$) correlation between Ht and Wt (0.29), Wt and BMI (0.91), WC (0.75) & HC (0.84). On the other hand all DXA results revealed positive significant ($p<0.001$) correlation anthropometric measurements Ht, Wt, BMI, WC and HC, the maximum very highly significant positive correlation was found between L1L4 and Wt, recorded 0.41. Concerning biomarkers indices of bone metabolism in selected women subjects, vitamin D showed negative significant correlation with Wt (-0.16, $p<0.05$)), WC (-0.18, $p< 0.01$),HC (-0.19, $p< 0.01$) and PTH(-0.18, $p< 0.01$), with positive significant correlation with Ht (0.14, $p< 0.05$), BMI (0.23, $p< 0.01$) and Ca (0.14, $p< 0.05$). on the other hand PTH showed positive significant ($p<0.05$) correlation with BMI (0.15), with negative significant ($p<0.001$) correlation to A.Ph (0.28). Positive significant ($p<0.001$) correlation between A.Ph and Mg (0.27), while negative significant ($p<0.01$) correlation Ca and (0.18) Mg was found.

DISCUSSION

The number of postmenopausal women have osteoporosis is set to rise with the aging of the population. The continued relevance of dietary intake and other nutritional factors in bone health are due, in part, to their potential for modification. The obvious influence of diet on bone health balance is of particular interest but has received insufficient attention in large-scale observational and intervention trials [12]. It is widely accepted that people over fifty years of age and postmenopausal women are at increased risk of developing osteoporosis due to accelerated bone loss, women are affected more so than men [13]. In present study the association between the calcium, vitamin D, PTH, and bone health were examined, as well as the axial and peripheral bone mass.

In our study the results found that most women have normal calcium level, while they have deficiency in vitamin D and hyperparathyroidism. The Saudi diet is characterized by excess sodium and chloride intake and lacks calcium [14]. Vitamin D is the most important factor in calcium absorption. Aging affects vitamin D formation, its produce with 50 % less as a result of decline renal function with aging [15]. Synthesis of vitamin D by the skin is reduced also due to less sun exposure and the skin capacity to produce vitamin D3 was decreased by more than two fold with aging [16]. Nevertheless, short-term sun light exposure might still benefit the synthesization of vitamin D in elderly people. Vitamin D deficiency causes malabsorption of calcium from the intestine. Therefore, taking calcium supplements together with vitamin D could improve the efficacy of calcium in preventing bone loss [15].

TABLE 4: Pearson correlation coefficients between anthropometric data, age of menarche, DMD and some biomarkers indices of bone metabolism

	Anthropometric data and age of menarche							**Biochemical bone indices**						**Bone mineral density (BMD)**				
	Ht (m)	Wt (kg)	BMI (Kg/m^2)	WC (cm)	HC (cm)	W/H (cm^2)	Age of menarche (Y)	Ca	Mg	A.Ph	PTH	Vit D	TC	L1L4	NK	WA	Tr	TF
Age (Y)	-0.23 [2]	-0.15 [1]	-0.06	0.02	-0.15[1]	0.18[2]	0.00	0.12	-0.03	-0.08	0.12	0.03	-0.06	-0.31[3]	- 0.36[3]	-0.39[3]	0.33[3]	-0.40[3]
Ht (m)		0.29[3]	-0.11	0.03	0.15[1]	-0.11	0.07	0.04	-0.01	0.10	-0.09	0.14[1]	0.02	0.25[3]	0.26[3]	0.22[3]	0.25[3]	0.21[2]
Wt (kg)			0.91[3]	0.75[3]	0.84[3]	0.06	-0.02	0.05	-0.06	0.01	0.11	-0.16[1]	0.10	0.41[3]	0.42[3]	0.39[3]	0.43[3]	0.43[3]
BMI (Kg/m^2)				0.76[3]	0.81[3]	0.10	-0.05	0.04	-0.06	-0.03	0.15[1]	0.23[2]	0.09	0.33[3]	0.32[3]	0.31[3]	0.34[3]	0.36[3]
WC (cm)					0.66[3]	0.60[3]	-0.01	-0.02	-0.05	-0.03	0.12	-0.18[2]	0.09	0.25[3]	0.26[3]	0.25[3]	0.27[3]	0.28[3]
HC(cm)						- 0.19[2]	-0.06	-0.01	-0.04	-0.02	0.06	-0.19[2]	0.07	0.31[3]	0.35[3]	0.34[3]	0.35[3]	0.36[3]
W/H (cm^2)							0.04	-0.02	-0.03	-0.03	0.08	-0.04	0.05	-0.001	-0.03	-0.03	-0.02	-0.02
Age of menarche (Y)								0.11	0.02	-0.01	-0.09	0.03	-0.04	-0.10	-0.06	-0.05	-0.02	-0.06
Ca (mmol/L)									-0.18[2]	0.09	-0.11	0.14[1]	0.17[1]	0.04	-0.11	-0.08	-0.10	-0.10
Mg (mmol/L)										0.27[3]	-0.03	-0.02	0.05	-0.06	-0.03	-0.03	-0.02	0.01
A.Ph mmol/L)											-0.28[3]	-0.04	0.04	0.06	0.11	0.13	0.07	0.09
PTH (pmol/L)												-0.18[2]	0.05	-0.10	-0.12	-0.10	-0.09	-0.10
Vit D(nmol/L)													-0.06	-0.07	0.001	-0.01	-0.02	-0.03
TC (mmol/L)														0.13	0.06	0.03	0.06	0.05
L1L4 (g/cm^2)															0.63[3]	0.64[3]	0.67[3]	0.69[3]
Nk (g/cm^2)																0.92[3]	0.86[3]	0.90[3]
WA (g/cm^2)																	0.88[3]	0.92[3]
Tr (g/cm^2)																		0.96[3]
TF(g/cm^2)																		

Ca: Calcium, Mg: Magnesium , A.ph: Alkaline Phosphates, PTH: Parathyroid hormone, TC: Total cholesterol, NK: Neck, WA: Wards, Tr: Troch, TF: Total femur. ([1]P<0.05, [2] P<0.01 and [3]P<0.001)

Calcium malabsorption occurs with aging, thus leads to negative calcium balance, hyperparathyroidism, increased bone loss, and osteoporosis. Data from clinical intervention trials demonstrate positive effects of long-term calcium supplementation may improve BMD and reduce fractures by suppressing PTH secretion as well as decreased bone resorption [17]. Parathyroid hormone act as regulator of calcium homeostasis and bone metabolism [18]. Continuously hyperparathyroidism activate osteoclasts with unknown negative impacts on bone [19].

In some studies hypercholesterolaemia has been associated with low BMD. In this study cholesterol level is above the accepted value for the same age and gender (<5.2 mmol/L). Orozco and colleagues [20] found that dyslipidemia postmenopausal women with had lower lumbar and femoral BMD and had an increased risk of osteopaenia compared to those with a normal lipid profile. Moreover, increase serum cholesterol level correlated with decrease in spine BMD independently of change in the BMI in postmenopausal women [21].

Age can predict the risk of fragility fractures in postmenopausal women independently of the level of BMD [22]. In this study there was negative significant (p<0.001) correlation between the BMD at the five bone site measured and age, with increasing age leading to decreasing BMD. The obtained results agree with a study of Beyazal et al. [23] which found a negative correlation between age and the BMD values for both femoral neck and lumbar spine. Sakondhavat et al.[24] and Li et al.[25] have stated that osteoporosis prevalence increases proportionally with increasing age and menopause duration in the lumbar vertebrae as well as the femoral neck. In postmenopausal women increasing age induce a significant decline in the vertebrae and femoral neck bone mass [26]. The loss in BMD occurs significantly in late perimenopause and is extremely rapid in the first postmenopausal year [27].

On the other hand the five points BMD measurements revealed positive significant (p<0.001) correlation anthropometric measurements. The fracture risk is higher in women with lower body weight compared to those with normal or higher body weight and similarly those being over their normal weight status are rarely affected by osteoporosis. The reasons for this are strengthening of the bones with increasing weight and protection from osteoporosis provided with estrogen metabolites produced by fat cells [28]. In a cross-sectional case-control study including 537 postmenopausal women, it was shown that BMI correlated positively with femoral neck and lumbar spine BMD [29].

Concerning biomarkers indices of bone metabolism in selected women subjects, vitamin D showed negative significant correlation with weight and PTH (p< 0.01). The obtained results agree with Aloia et al. [30] and Souberbielle et al. [31]. In addition Kharroubi et al. [32] found inverse correlation between vitamin D level and PTH. Vitamin D deficiency is one of the most common causes of secondary hyperparathyroidism [33]. It deficiency leads to defective calcium metabolism, defective osteoblastic activity, and defective matrix mineralization and finally leads to disorders of bone mineral density [34]. The increase in PTH due to a decrease in vitamin D that was not reflected dramatically on calcium levels that remained within the normal range is probably due to the effect PTH on bone and kidney and the effect of vitamin D on calcium absorption.

Moreover, PTH showed positive significant (p<0.05) correlation with BMI and obesity in Pearson correlation, which indicate that obesity is a risk factor for osteoporosis. The same result has been shown by other investigators [35-37]. It may be related to increasing weight and obesity constitutes a strong risk factor for diabetes, the associated low vitamin D levels, decreased insulin secretion, and or decreased insulin sensitivity contribute to the complexity of the effect of obesity on bone health [38].

Magnesium revealed negative significant (p<0.01) correlation with calcium, while no significant correlation with BMD. Magnesium through several mechanisms can effect on bone health. Also magnesium deficiency associates with the reduction of the levels of PTH and thus the decrease of vitamin D [39]. A meta-analysis by Farsinejad-Marj et al, were reported positive correlation between magnesium intake and bone mineral content, while others report no association [40].

In conclusion. Postmenopausal women have low BMD for the lumbar spine L1L4, neck, wards, troch, total femur. Several factors, such as age, duration of menopause, number of pregnancies, and BMI, affected the risk for osteoporosis. Public health promotional activities should be implemented in view of the relatively high prevalence

of osteoporosis. Further studies are needed on life style of postmenopausal women, as an influencing factors on osteoporosis prevalence and on prevention and management of primary osteoporosis.

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