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Research Article
Bone Health and its Relation to Energy Intake, Fat Mass and its Distribution

[1]Nayera E. Hassan, [1]Sahar A. El-Masry, [1]Rokia A. El Banna, [1]Muhammad Al-Tohamy, [2]Dalia El-Lebedy, [2]Dalia Adel Abdelhalim, [1]Darin Amin, [1]Safinaz Megahed and [1]Aya Khalil

[1]Department of Biological Anthropology, Medical Research Division, National Research Centre, 33 El-Buhouth Street, Dokki, Giza, 12622 Cairo, Egypt
[2]Department of Clinical and Chemical Pathology, Medical Research Division, National Research Centre, Cairo, Egypt

Abstract

Background and Objectives: Osteoporosis and obesity are two of the most important inter-related diseases worldwide. This study aimed to investigate impact of fat mass and its distribution on bone health in relation to energy intake among sample of Egyptian women. **Materials and Methods:** A cross-sectional study included 116 Egyptian women with age range 25-65 years old. They were classified according to the menopause into 2 groups: Pre-menopausal (n = 51) and post menopausal (n = 65). All participants have undergone anthropometric measurements, body composition, DEXA and laboratory investigations. **Results:** Among overweight/obese women, pre-menopausal women had significant higher values of BMR and BMD at both lumbar spines, neck of femur and significant lower values of central obesity (waist/hip ratio, waist/height ratio, visceral fat) and C-terminal peptides than postmenopausal ones. Among pre and post-menopausal women, BMD at both sites had significant positive correlations with obesity markers (BMI, waist and hip circumferences), fat mass, BMR, in addition to fat distribution, visceral fat, leptin among pre-menopausal women and C-terminal peptide among postmenopausal women. Among pre-menopausal women, BMR significantly explained 56% of the variations in BMD at neck of femur, while at lumbar spines the best model was BMI, BMR and waist circumference, which significantly explain 33% of the variations in BMD. **Conclusion:** Bone health positively correlated with BMI, fat mass and its distribution and BMR, particularly at femur neck, among pre and post-menopausal Egyptian women. Overweight/obesity can be considered as a protective factor for bone health.

Key words: Bone mineral density, body mass index, fat distribution, basal metabolic rate, visceral fat and leptin

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Corresponding Author: Sahar A. El-Masry, Department of Clinical and Chemical Pathology, Medical Research Division, National Research Centre, 33 El-Buhouth Street, Dokki, Giza, 12622 Cairo, Egypt

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Data Availability: All relevant data are within the paper and its supporting information files.

INTRODUCTION

Emerging evidence has revealed a close relationship between obesity and bone health[1]. Obesity is a complex disorder involving an abnormal or excessive amount of body fat[2]. Bone health is a reflection of bone mass, which is a measure of the amount of minerals (mostly calcium and phosphorous) contained in a certain volume of bone. Hence, it called bone density or Bone Mineral Density (BMD). Bone mass measurements are used to diagnose osteoporosis (a condition marked by decreased BMD), to see how well osteoporosis treatments are working and to predict how the bones are liable to break[3].

Obesity is associated with greater total body fat mass. Egypt Demographic and Health Survey (EDHS)[4] stated that the proportions classified as obese increased directly with age, from a level of 10% among women aged 15-19 to 65% or more among women aged 45-59. Urban women were more likely to be obese than rural women and the percentage classified as obese ranged from 25% in rural Upper Egypt to 49% in urban Lower Egypt. Women in the highest wealth quintile were almost twice, as likely as, women in the lowest quintile to be obese.

Studies have demonstrated that body fat and BMD were directly related, where mechanical loading, addition to other factors, may contribute to this relationship[5]. Moreover, dietary factors and physical activity might play a role. Adipocytes and osteoblasts originate from a common precursor; the pluripotent Mesenchymal Stem Cells (MSCs) of bone marrow[6].

Interestingly, some studies have found BMD to be positively associated with fat mass[7,8], whereas many others did not demonstrated this[9,10]. Most of these studies concerning postmenopausal women, rarely take into consideration pre-menopausal women. In Egypt, among postmenopausal women, Abd-Al-Atty[11] stated that while overweight was an independent protective factor for osteoporosis and regional fat percentage was not.

These studies, however, have focused on a specific sex, age, race or site of measurement, whereas few studies have compared the obesity paradox in pre- and post-menopausal women. Even though, patterns and occurrence of obesity, fat distribution and osteoporosis differed between pre- and post-menopausal women[12]. Therefore, different associations may be expected among pre- and post-menopausal women who have different lifestyles. Although awareness of some of the mechanisms through which fat and bone are correlated, this area is not fully understood. So, the aim of the present research was to investigate the impact of fat mass and its distribution on bone health (bone mass and its quality) in relation to energy intake (by assessing BMR) among a sample of pre- and post-menopausal women.

MATERIALS AND METHODS

One hundred and sixteen Egyptian obese women (with age range 25-65 years and a mean age 48.85±9.88 years) were included in this cross-sectional study. They were classified according to the menopause into 2 groups: Pre-menopausal (n = 51) and post menopausal (n = 65). Women were considered to be postmenopausal: if they were ≥55 years or reported as not having had a menstrual period during the past 12 months. A written informed consent was obtained from all participants after being informed about the purpose of the study.

Study area: They were recruited and randomly chosen, from all employees and workers of all categories of the National Research Centre, Egypt. This research paper was derived from a cross-sectional survey of a project funded by National Research Centre (NRC) Egypt, 2016-2019 entitled ''Bone mass among overweight and obese Women: Mechanism and Intervention.'' 11th Research Plan of the NRC, with an approval obtained from Ethics Committee of NRC (Registration Number is 16/127).

Anthropometric measurements: Body weight, height, waist and hip circumferences and skin fold thicknesses at 5 sites (triceps, biceps, sub scapular, suprailiac and abdominal) were measured, following the recommendations of the "International Biological Program"[13]. Body weight (Wt) was determined to the nearest 0.01 kg using a Seca Scale Balance, with the participant wearing minimal clothes and with no shoes. Body height (Ht) was measured to the nearest 0.1 cm using a Holtain portable anthropometer. Waist (WC) and Hip Circumferences (HC) were measured using non-stretchable plastic tape; approximated to the nearest 0.1 cm. WC was measured at the umbilicus level and HC at the level of the iliac crest; with the participant standing in an upright position. The skin fold thicknesses were measured at the left side using Holtain skin fold caliper and approximated to the nearest 0.1 mm.

The previously mentioned measurements were used to calculate the following parameters: Body Mass Index [BMI: weight (in kilograms) divided by height (in meters squared)], waist/hip ratio WHR (cm/cm), waist/height ratio WHtR (cm/cm), the peripheral adiposity index [sum of triceps and biceps skin fold thicknesses (mm)] and central adiposity index [sum of sub scapular, suprailiac and abdominal skin fold thicknesses (mm)].

Body composition: Body composition was assessed using the TANITA Body Composition Analyzer. As specified by the manufacturer, the unit was calibrated before testing. The participant stood on the foot board of the device, while she was holding the 2 handles carefully, each by one hand at the same time. By using her sex, age, weight and height, approximated to the nearest unit, the percentage body fat (Fat (%): an estimate of the fraction of the total body mass that is adipose tissue), Fat Mass (FM: an estimate of the fraction of the total body weight that is adipose tissue), Fat Free Mass (FFM: an estimate of the fraction of the total body weight that is not adipose tissue), body water content (liter), Basal Metabolic Rate (BMR in kilo calories: the rate at which the body uses energy, while at rest, to maintain vital functions such as breathing and keeping warm) and Visceral fat (Visceral fat is body fat that is stored in the abdominal cavity. Carrying excess body fat in this region places a person at greater risk for chronic diseases. For optimal health, visceral fat rating should stay under 13. Women with visceral fat values $\geq$13 are regarded as having visceral obesity, according to the machine instructions manual (Tanita Body Composition Analyzer-MC-780 MA III).

DEXA measurements: Both Bone Mineral Density "BMD" (g cm^{-2}) and BMD t-score at both the neck of femur and lumbar spines sites were measured using dual-energy DEXA (DEXA Norland XR-46 version 3.9.6/2.3.1, USA). Full body DEXA scan, based on the woman's age, weight and height, was performed with the participant keeping the precise distance between her arms and legs according to the machine instructions manual. A well-qualified operator executed and evaluated all analyses using the same protocol for all assessments.

Laboratory investigations: After overnight 8 h fasting, participants' venous blood samples were obtained by venipuncture in the morning to assess the following parameters: serum calcium (Ca), C-terminal peptide, IL6 and leptin. The blood samples that were left to clot were then centrifuged at 5000 rpm for 10 min to separate sera; that were then stored at -80°C to be assayed later on.

Serum calcium level was measured using the automated clinical chemistry analyzer Olympus AU 400 analyzer. Serum C-terminal peptide were measured using ELISA kit, E2 Catalogue number ES180S. Dal Biotech. The assay of human IL6 and Leptin in serum was performed by ELIZA method, BioLegend, Inc. 9727 Pacific Heights Blvd, San Diego, CA 92121, cat. No. 430504[14] and the kit of leptin were manufactured by Diagnostics biochem. Canada Inc (DBC). REF: CAN-L-4260[15].

The assessment of these parameters was done in the laboratory of Medical Excellence Research Center (MERC), which is part of National Research Centre (NRC), Egypt.

Statistical analysis: Data were analyzed using the Statistical Package for Social Sciences (SPSS/Windows Version 16, SPSS Inc., Chicago, IL, USA). Normality of data was tested using the Kolmogorov-Smirnov test. Most of the variables, such as; the data of DEXA, weight, BMI, visceral fat and calcium; were not normally distributed.

The 116 participant women were classified into 2 groups according to the menopause: pre-menopausal group (n = 51) and post-menopausal one (n = 65). The parametric data were expressed as median$\pm$SE, where the qualitative ones were expressed as number and percentage (%). The various variables of the 2 groups were analyzed and compared using Mann-Whitney test for independent groups.

Spearman's correlation coefficients were used to examine the correlation between BMD and the other variables in the present study. Stepwise regression analysis was also used to evaluate effect of different variable on BMD at femur neck and at lumbar spines. The p value ($p<0.05$) was regarded as statistically significant for all tests.

RESULTS

Comparative: Overweight/obese pre-menopausal and post-menopausal women had highly significant higher values than normal weight ones, in most of the anthropometric measurements under study (body weight, BMI, waist and hip circumferences and waist/height ratio), skin fold thickness at the 5 sites; peripheral and central fat and all body composition

Table 1: Comparison between different variables of overweight/obese and normal weight pre-menopausal women (using Mann-Whitney test)

	Overweight/obese (N = 35)		Normal weight (N = 16)		
Variables	Median	±SE	Median	±SE	p-value
Anthropometry					
Weight (kg)	85.10	3.46	53.40	0.66	0.000**
Height (cm)	158.00	1.00	153.00	0.56	0.008**
BMI (kg m^{-2})	35.04	1.10	22.81	0.41	0.000**
Waist circumference (cm)	96.00	2.06	80.50	1.94	0.000**
Hip circumference (cm)	118.00	1.88	91.50	0.75	0.000**
Waist/hip (cm cm^{-1})	0.83	0.01	0.88	0.03	0.051
Waist/height (cm cm^{-1})	0.62	0.01	0.53	0.01	0.000**
Skin fold thickness (mm)					
Biceps	25.00	1.09	21.50	1.76	0.006**
Triceps	30.00	1.76	22.00	2.00	0.001**
Sub scapular	30.50	1.52	19.50	0.59	0.000**
Supra iliac	24.00	1.37	12.00	0.96	0.000**
Abdominal	29.00	1.91	21.00	0.84	0.010**
Peripheral fat (mm)	55.00	2.33	45.00	3.67	0.002**
Central fat (mm)	78.75	3.57	52.00	2.08	0.000**
Body composition					
Fat (%)	44.30	1.05	24.70	1.05	0.000**
Fat mass (kg)	38.80	2.14	13.10	0.67	0.000**
Fat free mass (kg)	47.40	1.42	38.70	0.55	0.000**
Water (L)	34.70	1.00	28.30	0.40	0.000**
BMR (Kcal)	1472.00	28.88	1185.00	12.88	0.000**
Visceral fat rate	10.00	0.57	2.50	0.29	0.000**
DEXA					
Lumbar spines					
BMD (g cm^{-2})	1.03	0.04	0.87	0.02	0.003**
T-score	-0.37	0.16	-1.51	0.13	0.002**
Femur neck					
BMD (g cm^{-2})	0.88	0.03	0.73	0.02	0.000**
T-score	-1.02	0.22	-2.280	0.15	0.000**
Lab.					
Calcium (mg dL^{-1})	8.90	0.14	8.70	0.18	0.078
C-terminal peptide (pg mL^{-1})	940.00	160.65	917.50	71.95	0.467
IL6 (pg mL^{-1})	30.00	6.64	19.50	2.41	0.231
Leptin (ng mL^{-1})	16.00	1.86	1.65	2.10	0.001**

**p<0.01: Highly significant differences, negative sign implies that sample mean is less than the hypothesized mean

variables (Fat (%), fat mass, fat free mass, water, BMR and visceral fat). The laboratory investigations revealed that overweight/obese pre-menopausal women had the higher significant values of leptin than normal weight ones, while the overweight/obese postmenopausal women had the higher significant values of C-terminal peptide than normal weight ones (Table 1-2).

Overweight/obese pre-menopausal women were significantly taller had significant higher values of BMR, BMD and its T-score at both lumbar spines and neck of femur and significant lower values of central obesity (waist/hip ratio, waist/height ratio, visceral fat) and C-terminal peptides than overweight/obese postmenopausal women (Table 3).

Correlations: Among pre-menopausal women (Table 4), BMD at both lumbar spines and neck of femur had highly significant positive correlations with BMI, waist and hip circumferences, waist/height ratio, TSF, peripheral fat, all body composition variables and leptin. In addition, BMD at neck of femur had highly significant positive correlations with sub scapular and suprailiac skin fold thickness and central fat while BMD at lumbar spines had significant positive correlations with calcium.

Among postmenopausal women (Table 5), BMD at both lumbar spines and neck of femur had significant positive correlations with BMI, waist and hip circumferences and most of the body composition variables: Fat (%), fat mass, fat free mass, water and BMR. In addition, BMD at neck of femur had

Table 2: Comparison between different variables of overweight/obese and normal weight postmenopausal women (using Mann-Whitney test)

	Overweight/obese (N = 44)		Normal weight (N = 21)		
Variables	Median	±SE	Median	±SE	Mann-Whitney
Anthropometry					
Weight (kg)	83.95	2.29	56.10	1.23	0.000**
Height (cm)	155.50	1.13	158.00	1.33	0.213
BMI (kg m^{-2})	34.58	1.16	22.62	0.38	0.000**
Waist circumference (cm)	103.50	2.58	77.00	1.78	0.000**
Hip circumference (cm)	116.50	1.98	92.00	1.76	0.000**
Waist/hip (cm cm^{-1})	0.91	0.02	0.83	0.02	0.001**
Waist/height (cm cm^{-1})	0.68	0.02	0.47	0.01	0.000**
Skin fold thickness (mm)					
Biceps	25.50	1.10	13.00	1.37	0.000**
Triceps	30.00	1.51	20.00	1.42	0.000**
Sub scapular	27.50	1.67	20.00	1.03	0.000**
Supra iliac	27.50	1.08	20.00	1.38	0.000**
Abdominal	26.50	1.75	25.00	1.68	0.612
Peripheral fat (mm)	53.00	1.99	33.00	2.78	0.000**
Central fat (mm)	76.50	3.01	67.00	3.94	0.000**
Body composition					
Fat (%)	45.05	0.87	31.00	1.39	0.000**
Fat mass (kg)	38.25	1.74	16.50	1.08	0.000**
Fat free mass (kg)	45.05	0.73	38.40	0.38	0.000**
Water (L)	32.95	0.53	28.10	0.28	0.000**
BMR (Kcal)	1405.00	23.99	1174.00	11.18	0.000**
Visceral fat rate	11.50	0.53	6.00	0.33	0.000**
DEXA					
Lumbar spines					
BMD (g cm^{-2})	0.92	0.03	0.83	0.04	0.021*
T-score	-1.16	0.93	-1.54	0.25	0.067
Femur neck					
BMD (g cm^{-2})	0.77	0.02	0.70	0.01	0.004**
T-score	-1.96	0.16	-2.54	0.13	0.004**
Lab.					
Calcium (mg dL^{-1})	9.50	0.09	9.50	0.14	0.668
C-terminal peptide (pg mL^{-1})	1330.00	282.06	920.00	9.01	0.000**
IL6 (pg mL^{-1})	40.00	8.70	33.00	16.98	0.455
Leptin (ng mL^{-1})	15.00	1.48	15.00	2.26	0.749

*p<0.05: Significant differences, **p<0.01: Highly significant differences, negative sign implies that sample mean is less than the hypothesized mean

highly significant positive correlations with visceral fat, while BMD at lumbar spines had significant positive correlations with waist/height ratio and C-terminal peptide. There were insignificant correlations between BMD at both sides and body fat distribution; peripheral or central; calcium, leptin or IL6.

Regression: Stepwise regression analysis (Table 6), evaluated the effect of BMI, WC, HC, Waist Height Ratio (WHtR), peripheral obesity, central obesity, fat mass, visceral fat and BMR on BMD at neck of femur and it has revealed that BMR significantly explain 56% of the variations in BMD at neck of femur among pre-menopausal women, while visceral fat significantly explain 9% of the variations in BMD at neck of femur among postmenopausal women. Regression analysis excluded the other variables.

Stepwise regression analysis to evaluate effect of different variable on BMD at lumbar spines (Table 7), revealed that the best model was BMI, BMR and waist circumference which significantly explain 33% of the variations in BMD at lumbar spines among pre-menopausal women, while BMR significantly explain 9% of the variations in BMD at lumbar spines among postmenopausal women. Regression analysis excluded the other variables.

DISCUSSION

Various studies well established that obesity has a protective effect against osteoporosis, through playing an important role in protecting BMD and bone quality[16,17]. In agreement with this observation, the current study revealed that overweight/obese pre-menopausal and post-menopausal

Table 3: Comparison between different variables of overweight/obese pre-menopausal and post-menopausal women (using Mann-Whitney test)

	Pre-menopausal women (N = 35)		Post-menopausal women (N = 44)		
Variables	Median	±SE	Median	±SE	p-value
Anthropometry					
Weight (kg)	85.10	3.46	83.95	2.29	0.433
Height (cm)	158.00	1.00	155.50	1.13	0.048*
BMI (kg m^{-2})	35.04	1.10	34.58	1.16	0.820
Waist circumference (cm)	96.00	2.06	103.50	2.58	0.051
Hip circumference (cm)	118.00	1.88	116.50	1.98	0.711
Waist/hip (cm cm^{-1})	0.83	0.01	0.91	0.02	0.001**
Waist/height (cm cm^{-1})	0.62	0.01	0.68	0.02	0.006**
Skin fold thickness (mm)					
Biceps	25.00	1.09	25.50	1.10	0.957
Triceps	30.00	1.76	30.00	1.51	0.843
Sub scapular	30.50	1.52	27.50	1.67	0.283
Supra iliac	24.00	1.37	27.50	1.08	0.197
Abdominal	29.00	1.91	26.50	1.75	0.266
Peripheral fat (mm)	55.00	2.33	53.00	1.99	0.929
Central fat (mm)	78.75	3.57	76.50	3.01	0.468
Body composition					
Fat (%)	44.30	1.05	45.05	0.87	0.468
Fat mass (kg)	38.80	2.14	38.25	1.74	0.949
Fat free mass (kg)	47.40	1.42	45.05	0.73	0.111
Water (L)	34.70	1.00	32.95	0.53	0.105
BMR (Kcal)	1472.00	28.88	1405.00	23.99	0.031*
Visceral fat rate	10.00	0.57	11.50	0.53	0.017*
DEXA					
Lumbar spines					
BMD (g cm^{-2})	1.03	0.04	0.92	0.03	0.030*
T-score	-0.37	0.16	-1.16	0.93	0.014*
Femur neck					
BMD (g cm^{-2})	0.88	0.03	0.77	0.02	0.001**
T-score	-1.02	0.22	-1.96	0.16	0.001**
Lab.					
Calcium (mg dL^{-1})	8.90	0.14	9.50	0.09	0.093
C-terminal peptide (pg mL^{-1})	940.00	160.65	1330.00	282.06	0.003**
IL6 (pg mL^{-1})	30.00	6.64	40.00	8.70	0.078
Leptin (ng mL^{-1})	16.00	1.86	15.00	1.48	0.492

*p<0.05: Significant differences, **p<0.01: Highly significant differences, negative sign implies that sample mean is less than the hypothesized mean

women had the higher values of BMD and the lower values of t-score at both lumbar spines and neck of femur than normal weight ones. In contrast, some studies showed high risk of fracture and osteoporosis in obese people[18]. They attributed this to the adverse affects of obesity on bone health by a variety of mechanisms; such as an alteration of bone-regulating hormones, increased oxidative stress and inflammation and altered bone cell metabolism[19]. While some researchers have reported that, the increase in fat mass and adipose tissue was not beneficial for bone density[20-22].

Current results indicated that among the over weight/obese women, there were insignificant differences between the pre and post-menopausal groups in fat mass or distribution. While the obese pre-menopausal women had significant higher values of BMR and BMD and the obese post-menopausal women had significant higher values of central obesity and C-terminal peptides. Among pre and post-menopausal women, BMD at both sites had highly significant positive correlations with obesity markers (BMI, waist and hip circumferences), fat mass, BMR, in addition to body fat distribution, visceral fat and leptin among pre-menopausal women only. While among postmenopausal women, BMD at neck of femur had highly significant positive correlations with visceral fat. Among pre-menopausal women, BMR significantly explains 56% of the variations in BMD at neck of femur, while BMI, BMR and waist circumference was the best model, which significantly explained 33% of the variations in BMD at lumbar spines. Among post-menopausal women, BMR also significantly explained 9% of the variations in BMD at lumbar spines, while visceral fat significantly explain 9% of the variations in BMD at femur neck. Regression analysis excluded the other variables.

Table 4: Spearman's correlations between BMD and different variables among pre-menopausal women

	BMD among pre-menopausal			
	At lumbar spines		At femur neck	
Variables	r	p	r	p
Anthropometry				
BMI (kg m^{-2})	0.560**	0.000	0.762**	0.000
Waist circumference (cm)	0.460**	0.001	0.685**	0.000
Hip circumference (cm)	0.411**	0.003	0.721**	0.000
Waist/hip (cm cm^{-1})	-0.001	0.994	-0.050	0.730
Waist/height (cm cm^{-1})	0.469**	0.001	0.599**	0.000
Skin fold thickness (mm)				
Biceps	0.177	0.213	0.263	0.062
Triceps	0.353*	0.011	0.359**	0.010
Sub scapular	0.251	0.079	0.399**	0.004
Supra iliac	0.263	0.062	0.444**	0.001
Abdominal	0.126	0.377	0.143	0.316
Peripheral fat (mm)	0.345*	0.013	0.347*	0.013
Central fat (mm)	0.274	0.054	0.405**	0.004
Body composition				
Fat (%)	0.507**	0.000	0.743**	0.000
Fat mass (kg)	0.514**	0.000	0.760**	0.000
Fat free mass (kg)	0.386**	0.005	0.739**	0.000
Water (L)	0.387**	0.005	0.738**	0.000
BMR (Kcal)	0.412**	0.003	0.782**	0.000
Visceral fat rate	0.448**	0.001	0.663**	0.000
Lab.				
Calcium (mg dL^{-1})	0.359*	0.011	-0.023	0.876
C-terminal peptide (pg mL^{-1})	- 0.048	0.743	-0.086	0.557
IL6 (pg mL^{-1})	- 0.061	0.677	0.125	0.394
Leptin (ng mL^{-1})	0.432**	0.002	0.368**	0.009

*p<0.05: Significant differences, **p<0.01: Highly significant differences

There are biological reasons to explain why overweight can actually protect from osteoporosis: first, excess body weight predisposes the body to mechanical loading, which is crucial for bone health[23]. Second, in post-menopausal women, the aromatization of androgens into estrogens occurs in lean and fat tissue and is the major source of natural estrogen, which may explain some of the positive relationship between post-menopausal bone density and body weight[24,25]. Third, adiposity-regulating hormones have clear effects on BMD; leptin is associated positively with BMD, whereas adiponectin shows a negative relationship[26].

Actually, according to current findings, leptin values of overweight/obese pre-menopausal women were significantly higher than among normal weight ones. Although, some studies have shown a positive association between leptin and BMD[27,28], yet other studies reported no significant association[29] or even a negative association[30]. It has been suggested that, leptin may play a mediating role in maintaining bone mass in obese people[31]. It has been shown that leptin promotes bone formation by increasing human osteoblast proliferation, collagen synthesis and mineralization[32]. Moreover, other studies found that leptin inhibits osteoclast generation and bone resorption[33].

In the present study overweight/obese postmenopausal women had recorded higher values of C-terminal peptide than normal weight ones. Similarly, Seifert-Klauss *et al.*[34] have found, that significantly higher levels of β-CTX in postmenopausal women consistent with previous reports indicating that significant bone density loss was associated with a rapid increase in C-terminal peptide among menopausal women.

The impact of fat mass on BMD differs according to fat distribution[35]. In this study, among pre-menopausal women, highly significant positive correlations were observed between BMD at lumbar spines and peripheral fat distribution, while at neck of femur with both peripheral and central fat distribution and with waist/height ratio at both of lumbar spines and at neck of femur. Among postmenopausal women, BMD at lumbar spines had highly significant positive correlations with waist/height ratio and with visceral fat at neck of femur.

Generally, the results of subcutaneous fat thickness which to be assessed using Skin Fold Thickness (SFT) and bone in observational studies are somewhat controversial. Similar to current analysis positive associations between SFT and bone mass[35], however, negative association was reported in another study by Katzmarzyk *et al.*[36].

Table 5: Spearman's correlations between BMD and different variables among postmenopausal women

	BMD among post menopausal women			
	At lumbar spines		At femur neck	
Variables	r	p	r	p
Anthropometry				
BMI (kg m^{-2})	0.294*	0.017	0.280*	0.024
Waist circumference (cm)	0.327**	0.008	0.295*	0.017
Hip circumference (cm)	0.285*	0.021	0.318**	0.010
Waist/hip (cm cm^{-1})	0.166	0.186	0.128	0.311
Waist/height (cm cm^{-1})	0.299*	0.016	0.238	0.056
Skin fold thickness (mm)				
Biceps	0.169	0.179	0.150	0.234
Triceps	0.105	0.405	0.225	0.072
Sub scapular	-0.108	0.391	0.115	0.362
Supra iliac	0.228	0.068	0.205	0.101
Abdominal	-0.236	0.058	0.007	0.958
Peripheral fat (mm)	0.129	0.305	0.230	0.065
Central fat (mm)	-0.077	0.542	0.169	0.179
Body composition				
Fat (%)	0.293*	0.018	0.301*	0.015
Fat mass (kg)	0.314*	0.011	0.330**	0.007
Fat free mass (kg)	0.355**	0.004	0.421**	0.000
Water (L)	0.354**	0.004	0.421**	0.000
BMR (Kcal)	0.349**	0.004	0.388**	0.001
Visceral fat rate	0.211	0.091	0.377**	0.002
Lab.				
Calcium (mg dL^{-1})	0.058	0.657	0.110	0.400
C-terminal peptide (pg mL^{-1})	0.322*	0.014	0.231	0.082
IL6 (pg mL^{-1})	-0.082	0.541	0.016	0.904
Leptin (ng mL^{-1})	-0.089	0.508	0-.100-	0.456

*p<0.05: Significant differences, **p<0.01: Highly significant differences

Table 6: Stepwise regression analysis to evaluate effect of different variable on BMD at neck of femur

				Unstandardized coefficients		
Menopause class		R	R^2	B	Std. error	Significance
Pre-menopausal	Constant			0.015	0.106	0.886
	BMR (Kcal)	0.746[a]	0.556	0.001	0.000	0.000**
Post-menopausal	Constant			0.678	0.035	0.000**
	Visceral fat	0.298[b]	0.089	0.008	0.003	0.016*

*p<0.05: Significant differences, **p<0.01: Highly significant differences, a showed significant variation in BMR, b showed significant variation in visceral fat

Table 7: Stepwise regression analysis to evaluate effect of different variable on BMD at lumbar spines

				Unstandardized coefficients			
Menopause class		R	R^2	B	Std. error	Significance	Model significance
Pre-menopausal	Constant			1.468	0.242	0.000	0.000**
	BMI	0.387	0.150	0.034	0.008	0.000	
	BMR (Kcal)	0.511	0.261	0.000	0.000	0.021	
	WC (cm)	0.572	0.327	-0.006	0.003	0.038	
Menopausal	Constant			0.506	0.184	0.008	0.040*
	BMR (Kcal)	0.256	0.065	0.000	0.000	0.040	

*p<0.05: Significant differences, **p<0.01: Highly significant differences

Liu *et al.*[12] demonstrated that higher amounts of Visceral Adipose Tissue (VAT) are associated with greater BMD and better microstructure of the peripheral skeleton. Also, current results confirmed these findings, where BMD at neck of femur had highly significant positive correlations with visceral fat. Whereas, some studies contrasts that and found negative relationship between VAT and BMD[36-40].

In the present study, obesity was more strongly correlated with BMD at femoral sites, compared with those at the lumbar spine. Femoral sites are composed of relatively higher cortical bones than the lumbar spine[41]. Thus, these findings suggest that body composition parameters may have a greater effect on cortical bone than trabecular bone, similar to observations by Ahn *et al.*[42].

By focusing specifically on BMR, current study showed that pre-menopausal women had recorded higher values and lesser affection of osteoporotic changes than postmenopausal in femur and spine. This finding suggested that the effects of BMR may have a substantial effect on the skeleton BMD. In agreement with the current results, Hsu *et al.*[43] and Choi and Pai[44] have reported that BMR is closely associated with BMD in elderly persons (non-osteoporotic had higher BMR). The BMR may be a novel target for interventions aimed at preventing the age-related decline in BMD.

Choi and Pai[44] concluded that, in postmenopausal women, BMD is strongly correlated with BMR and that BMD of the lumbar spine was more strongly correlated with BMR ($r = 0.51$, $p<0.01$) than with lean body mass ($r = 0.39$, $p<0.01$) and waist/hip ratio ($r = -0.28$, $p<0.01$). Moreover, in osteoporotic women, the mean values of BMR were significantly lower than those for non-osteoporotic ones ($p<0.01$). In agreement with current results they found that BMR, in elderly persons, strongly correlates with BMD compared to TBF, BMI or lean body mass.

Hedlund and Gallagher[45] concluded that menopause correlates with decreased BMD at several skeletal sites, although not previously been observed in the hip. Moreover, in the early postmenopausal years, BMD decreased faster at all sites, where the decrease in BMD of the femoral neck and trochanter, during the first 6 years postmenopausal was 3-10 times higher than in the decade prior to menopause[45]. These findings confirm that the combined effect of both age and menopause represent major factors of low BMD, a risk factor for osteoporosis[45-46].

CONCLUSION

Bone health is significantly positively correlated with body mass index, fat mass and its distribution and BMR, particularly at femur neck; among pre and post-menopausal women. Moreover, it is significantly positive correlated with leptin among pre-menopausal women and with C terminal peptide among postmenopausal women.

So, overweight/obesity can be considered as a protective factor for bone health. Central obesity determined by WHtR not WHR; can be considered as easy diagnostic important tool in assessment of bone health among pre and post-menopausal women.

SIGNIFICANCE STATEMENT

This study discovers the possible synergistic effect of BMR, fat mass and its distribution that can be beneficial for bone health. It also throw light on the combined effect of both age and menopause, which represent major factors of low BMD and osteoporosis. It will help the researcher to uncover the critical area of postmenopausal bone loss that many researchers were not able to explore. Thus, a new theory on the combination of BMR, fat mass, its distribution and possibly other combinations, may be arrived at.

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