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Influence of Overweight and Obesity on Bone Mineral Density in Egyptian Premenopausal Women

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ABSTRACT

Background and objective: Can overweight and obesity exert a detrimental or a protective effect on bone density in premenopausal women? We studied the correlation between obesity and bone mineral density (BMD) in premenopausal women in Egypt. **Patients and methods:** a Case-control study included 50 overweight and obese premenopausal women compared to 50 normal weight women of matched age. Clinical history, examination, laboratory tests and DEXA scan were done. **Results:** T–score and Z-score at the forearm, hip, and lumbar vertebrae were significantly lower in the case group than the control group. In all participants, we found a significant negative correlation between body mass index (BMI) with Z-score (forearm), BMI and bodyweight with Z-score (hip) and BMI, waist circumference (WC) and bodyweight with Z-score (lumbar vertebrae). We found a significant negative correlation between waist/ hip ratio (WHR) and T-score (hip) and between BMI, waist/hip ratio and bodyweight with T-score (lumbar vertebrae). In the overweight and obese participants, BMI was inversely correlated with Z-score (forearm, hip, and lumbar vertebrae) as well as waist circumference with Z-score (lumbar vertebrae). With post-hoc analysis, T-score at the lumbar vertebrae was significantly lower in the obese group. With adjustment of the age, (age and WC) and (age and WHR), we found a significant negative association in the obese group versus the lean group with Z-score (forearm, hip and lumbar vertebrae).

Conclusion: Overweight and obese Egyptian premenopausal women were more vulnerable to lower bone density.

Keywords: Bone mineral density, Obesity, Premenopausal women.

INTRODUCTION

Obesity and osteoporosis threaten human health and are strictly related to growing incidence of morbidity and mortality worldwide [(1)]. Obesity is a complex disorder with abnormal excessive fat deposition [(2)]. Osteoporosis is a disorder of deranged bone strength with a higher fracture risk. Integration of bone density and quality is essential for bone strength which is identified through Bone Mineral Density (BMD) assessment. Osteoporosis is often overlooked and undertreated due to its silent course before fracture occurs [(3)]. The gold standard method to assess bone mineral density (BMD) is Dual-energy X-ray absorptiometry (DEXA) [(4)].

WHO defined osteoporosis of BMD 2.5 standard deviations or more lower than the average value for young healthy women (T-score $\leq$ -2.5 SD) [(5)]. Both adipocyte and osteocyte originate from the same stem cell representing unexplained close interrelation between adipose tissue and bone [(6)]. The correlation between obesity and osteoporosis is still controversial; some researchers found a protective effect of obesity against osteoporosis "obesity paradox" [(7, 8)]. However others considered obesity as a risk factor for osteoporosis [(9, 10)]. Different associations may be expected in premenopausal women as they have a different pattern of fat distribution, lifestyle and bone density than others. In Egypt, there is a lack of data about the effect of obesity on BMD in premenopausal women. Therefore, we tried to get a delicate assessment of the relationship between obesity and BMD in premenopausal women in Egypt.

PATIENTS AND METHODS

This is an observational case-control study conducted at the outpatient department at our institution during the period from December 2018 to May 2019. The study included 50 obese premenopausal women compared with 50 normal-weight women of matched age as a control group. The case group comprised 50 women of age (31-39 years old) with BMI (25 – 40 kg/m²).

Exclusion criteria: we excluded patients with chronic diseases (diabetes, hypertension, ischemic heart diseases, chronic obstructive pulmonary disease, renal, hepatic diseases, or endocrinal disorders), nutritional disorders or autoimmune diseases, patients on medications affecting bone metabolism like diuretics, steroid, calcium, or hormones and patients with prior bariatric surgery.

All participants were subjected to detailed clinical history and examination with anthropometric measurements; body weight, height, body mass index (BMI) waist circumference and waist/hip ratio (WHR) [(11)]. Laboratory tests for assessment of fasting blood glucose (FBS), postprandial blood sugar (PPBS) [(12)], lipid profile [(13)], serum calcium, phosphorus, vitamin D3, intact parathyroid hormone, renal, hepatic function

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tests, serum uric acid [14] and thyroid function tests [15]. Dual-energy X-ray absorptiometry (DEXA) scan was done by the General Electric DEXA scan, DEXA bone densitometer/pencil beam Lunar DPX NT, Germany [4].

Ethical Approval and consent to participate:

This study was approved by the Institutional Review Board for Clinical Research Committee of Mansoura University with approval number (No.R.18.6.541). All procedures performed in studies involving human participants were in accordance with the ethical standards of the Institutional Research Committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. Written informed consent was approved by the Institutional Review Board for Clinical Research Committee of Mansoura University and obtained from all participants.

Statistical analysis: data were analysed with SPSS (version 20); Description of quantitative variables e.g. frequency, mean ±SD, median, and range while qualitative variables as number percentage. Comparison between two groups for the quantitative variable in parametric data was done with unpaired t-test with significant p-value of less than 0.05.

RESULTS

Table (1) shows demographic data of the participants; body weight, BMI, waist circumference, and triglycerides were significantly higher in the case group than the control group.

Table (1): Baseline clinical and laboratory data of studied groups

Characters	Cases (n=50)	Control (n=50)	P value
Age (year)	35.0±3.4	34.1±3.8	>0.05
Weight (kg)	92.2±13.9	67.7±5.7	<0.001
Height (cm)	160.9±6.2	163.10 ± 6.14	>0.05
Waist Circumference (cm)	116.2±11.8	96.3±9.4	<0.001
Hip Circumference (cm)	121.0±8.9	110.2±7.4	<0.001
Waist Hip Ratio	0.96±0.11	0.87±0.06	<0.001
BMI (kg/ m²)	35.4±4.4	22.9±3.9	<0.001
Normal (<25)	0(0%)	50(100%)	<0.001*
Overweight (25-30)	6(12%)	0(0%)	
Obesity (30-40)	34(68%)	0(0%)	
Morbid obese (40-50)	10(20%)	0(0%)	
Total cholesterol (mg/dl)	181.9±34.5	178.2±28.9	>0.05
Triglyceride (mg/dl)	144.2±25.9	113.9±19.3	<0.001
HDL-C(mg/dl)	42.0±8.1	57.7±6.8	<0.001
LDL-C (mg/dl)	101.0±21.1	97.7±23.8	>0.05

Table (2) shows DEXA scan of study participants.

Table (2): DEXA scan parameters of studied groups.

Characters	Cases (n=50)	Control (n=50)	P value
Z score forearm	-0.1 (-1.6:0.9)	0.5 (-1.1:2.5)	0.035
Z score hip	-0.2 (-2.1:1.9)	0.3 (-0.9:2.9)	0.005
Z score lumbar vertebrae	-0.9 (-2.9:1.7)	-0.1 (-1.1:2.0)	<0.001
T score forearm	-0.1 (-1.6:1.1)	0.5 (-1.2:2.5)	0.018
T score hip	-0.1 (-1.7:2.5)	0.5 (-0.8:2.5)	0.010
T score lumbar vertebrae	-0.2 (-1.6:1)	0.2 (-0.6:2.7)	0.004

In all participants, there was a significant negative correlation between BMI and Z-score at forearm, BMI and body weight with Z-score at the hip and between BMI, waist circumference and bodyweight with Z-score at lumbar vertebrae (Table 3).

Table (3): Correlation between body fat parameters with different Z-score in all study participants

Predictor	Z score forearm		Z score hip		Z score lumbar vertebrae	
	r	p	r	p	r	p
BMI	-0.261	0.009	-0.317	0.001	-0.534	< 0.001
Waist circumference	-0.041	0.684	-0.165	0.101	-0.404	< 0.001
Waist hip ratio	-0.004	0.967	-0.037	0.714	-0.025	0.806
Weight	-0.176	0.080	-0.280	0.005	-0.542	< 0.001

Also we found a significant negative correlation between BMI, waist / hip ratio (WHR) and bodyweight with T- score at lumbar vertebrae in all participants (Table 4).

Table (4): Correlation between body fat parameters with different T-score in all study participants

Predictor	T score UL		T score LL		T score lumbar vertebrae	
	r	p	r	P	R	p
BMI	-0.194	0.054	-0.178	0.076	-0.290	0.003*
Waist circumference	-0.044	0.664	0.038	0.707	-0.194	0.053
Waist hip ratio	-0.121	0.230	-0.197	0.049*	-0.282	0.004*
Weight	-0.137	0.173	-0.094	0.353	-0.222	0.026*

In overweight and obese group, there was a significant negative correlation between BMI and Z-scores forearm, hip, and lumbar vertebrae (Table 5).

Table (5): Correlation between obesity parameters with Z-score in the obese and overweight group.

Predictor	Z score forearm		Z score hip		Z score Lumbar vertebrae	
	r	p	r	p	r	P
BMI	-0.356	0.036	-0.398	0.004	-0.406	0.003
Waist circumference	-0.228	0.111	-0.042	0.771	-0.319	0.024
Waist hip ratio	-0.155	0.282	-0.048	0.739	-0.037	0.799
Weight	0.169	0.239	-0.264	0.064	-0.385	0.06

With categorization of all participants according to BMI, there was a significant difference between the obese and normal weight groups as regards the association between BMI and T- score at the hip and lumbar vertebrae where BMD was significantly lower in obese group (Table 6).

Table (6): Relationship between BMI and T score in total sample

	BMI (kg/m^2)				H	p
	Normal (<25) (n= 32)	Overweight (25-30) (n= 11)	Obesity (30-40) (n= 41)	Morbid obese (40-50) (n= 16)		
T score UL						
Min. – Max.	-1.20 – 2.50	-1.00 – 0.60	-1.60 – 1.10	-1.20 – 0.70		
Mean ± SD.	0.13 ± 0.96	-0.18 ± 0.57	-0.24 ± 0.75	-0.40 ± 0.64	5.873	0.118
Median	0.50	-0.15	-0.10	-0.40		
Tscore LL						
Min. – Max.	-0.80 – 2.50	-1.20 – 1.30	-1.70 – 2.30	-0.80 – 2.50		
Mean ± SD.	0.82 ± 1.04	0.10 ± 0.93	0.22 ± 0.99	0.45 ± 1.02	6.894	0.075
Median	0.50	0.30	0.15	0.10		
T score lumbar vertebrae						
Min. – Max.	-0.60 – 2.70	-1.30 – 1.00	-1.60 – 0.90	-0.40 – 1.00		
Mean ± SD.	0.29 ± 0.72	0.03 ± 0.92	-0.33 ± 0.67	0.19 ± 0.44	13.602	0.004*
Median	0.20	0.35	-0.35	0.10		
Sig.bet.Grps	p_1=0.735, p_2<0.001*, p_3=0.887, p_4=0.142, p_5=0.851, p_6=0.038*					

†H: H for Kruskal-Wallis test, Pairwise comparison between each 2 groups was done using Post Hoc Test (Dunn's for multiple comparisons test).

¶p: p value for association between BMI (kg/m^2) and T score.
¶p_1: p value for association between normal and overweight.
¶p_2: p value for association between normal and obesity.
¶p_3: p value for association between normal and morbid obese.
¶p_4: p value for association between overweight and obesity.
¶p_5: p value for association between overweight and morbid obese.
¶p_6: p value for association between obesity and morbid obese.
*: Statistically significant at $p \le 0.05$.

Simple linear regression analysis revealed a significant negative association of overweight and obese group versus the lean group with Z-score at forearm, hip and lumbar vertebrae after adjustment of age, (age and waist circumference) and (age and waist-hip ratio) (Table 7).

Table (7): Association between obesity and overweight with different Z scores

	Model	Z- score forearm		Z -score hip		Z -score lumbar vertebrae	
		B (95% CI)	p	B (95% CI)	P	B (95% CI)	p
Cases Control	**Crude**	-0.72 (-1.24:-0.20) = Rc	0.007 RC	-0.67 (-1.09:-0.26) RC	0.002 RC	-0.68 (-1.03:-0.32) RC	<0.001 RC
Cases Control	**Model 1**	-0.50 (-0.91:-0.09) = RC	0.017 RC	-0.61 (-1.08:-0.14) RC	0.011 RC	-0.55 (-0.95:-0.15) RC	0.008 RC
Cases Control	**Model 2**	-0.11 (-0.83:0.61) = RC	0.760 RC	-0.17 (-1.08:0.73) RC	0.704 RC	-0.23 (-0.98:0.53) RC	0.552 RC
Cases Control	**Model 3**	-0.36 (-0.70:-0.03) = RC	0.034 Rc	-0.88 (-1.53:-0.22) RC	0.009 RC	-0.58 (-1.14:-0.02) RC	0.043 RC
Cases Control	**Model 4**	-0.44(-0.82:-0.06) = RC	0.023 RC	-0.77 (-1.28:-0.26) RC	0.004 RC	-0.67 (-1.11:-0.24) RC	0.003 RC
Cases Control	**Model 5**	-0.23 (-0.76:0.29) =RC	0.382 RC	-0.30 (-0.95:0.35) RC	0.361 RC	-0.17 (-0.72:0.38) RC	0.545 RC

¶Model (1): age adjusted.
¶Model (2): age, BMI adjusted.
¶Model (3): age, waist circumference adjusted.
¶Model (4): age, waist hip ratio adjusted.
¶Model (5): age, weight adjusted.
RC= Regression calibration

DISCUSSION

In our study, T-score and Z-score at (forearm, hip and lumbar vertebrae) were significantly lower in the case group than the control group. We found a significant negative correlation between obesity parameters and BMD indices such as BMI with Z-score at (forearm, hip, and lumbar vertebrae), waist circumference and Z-score at lumbar vertebrae as well as BMI, waist / hip ratio (WHR) and bodyweight with T- score at lumbar vertebrae

Despite ethnicity variation, our findings agreed with other researchers who found an inverse relationship between body fat mass and bone density in contrary to the lean mass which showed a consistent positive correlation with bone density. Therefore, bone density did not gain benefit from increased adipose tissue mass in premenopausal women [16-18]. Also, **Kim *et al.*** [19] found an inverse relationship between obesity indices with BMD throughout all age groups including premenopausal women.

Sue *et al.* [20] attributed the deleterious influence of obesity on bone health to the bone-regulating hormones disturbance, chronic inflammation, oxidative stress and disordered endocannabinoid system integrity. Also, **Savvidis *et al.*** [21] found that the obese individuals are more vulnerable to fractures due to deteriorated bone integrity induced by the chronic inflammation associating abdominal obesity.

Simple linear regression analysis of our data revealed a significant negative association between obesity and Z-score at (forearm, hip and lumbar vertebrae) after adjustment of age, (age and WC) and (age and WHR) in the obese versus the lean groups.

Also, **Lekamwasam *et al.*** [22] considered the lean mass as the most powerful predictor of bone mineral density as well as **Kim *et al.*** [23], who found that the subcutaneous and visceral fat mass negatively affected BMD after BW adjustment while the lean mass was positively correlated with BMD regardless of body weight.

Our results agreed with **Kim *et al.*** [24], who found an inverse correlation between WHR and lumbar vertebrae BMD which was positively correlated with the lean mass in perimenopausal Korean women as well as **Kim *et al.*** [25]**,** who adjusted BMI and found a negative correlation between fat mass and bone density.

Femur and spine BMD was negatively correlated with the fat mass after lean mass adjustment through mechanical load decrease [18]. BMD improved with body weight decline; therefore weight loss may alleviate fracture risk. The deleterious effect of weight-adjusted fat mass on bone might be driven by increased pro-inflammatory cytokines, which may activate the receptors of nuclear factor-κB ligand, enhancing bone resorption [26].

Also, **Blum *et al.*** [27] found a negative correlation between the body fat mass and BMD of the (hip, lumbar spine and total body) particularly with elevated leptin levels in premenopausal women that coincided with our results.

On the other hand, **Alshafei *et al.*** [28], found a positive correlation between BMI and BMD in premenopausal women but they had a very small sample size (20 patients only). **Shi and Baldock** [29] found a significant reduction of neuropeptide Y (NPY) expression that activates the osteoblasts with strengthening the skeleton in the obese individuals.

However, **Douchi *et al.*** [30] differentiated the pattern of fat distribution and found that upper body fat mass rather than the whole body adiposity affects BMD at lumbar spine in premenopausal women.

However, this inconsistency may be attributed to the variations in the study methodology, sample size, ethnicity, genetics, research designs and sampling modality.

Our main strength point was the clarification of the correlation between various obesity parameters with DEXA indices (T-score and Z score) at different body sites, while our main limitations were the single-center trial and ethnicity. Future studies with larger-scale of multi-ethnicities with long term follow up are warranted in the future.

CONCLUSION

Egyptian premenopausal women with overweight and obesity are more vulnerable to a lower bone mineral density than lean peers, therefore; they should attain normal weight to preserve their BMD and to minimize fracture risk.

Conflict of interest: nil

REFERENCES

1. **Greco E, Lenzi A, Migliaccio S (2015):** The obesity of bone. Ther. Adv. Endocrinol. Metab., 6: 273–286.
2. **Palermo A, Tuccinardi D, Defeudis G *et al.* (2016):** BMI and BMD: The potential interplay between obesity and bone fragility. Int J Environ Res Public Health, 13(6): 544.
3. **Khadilkar A, Mandlik R (2015):** Epidemiology and treatment of osteoporosis in women: An Indian perspective. Int J Women's Health, 7:841–850.
4. **Lewiecki E, Binkley N, Morgan S *et al.* (2016):** Best practices for dual-energy x-ray absorptiometry measurement and reporting: International Society for Clinical Densitometry Guidance. Journal of Clinical Densitometry: Assessment & Management of Musculoskeletal Health, 19 (2): 127–140.
5. **Shuler F, Conjeski J, Kendall D *et al.* (2012):** Understanding the burden of osteoporosis and use of the World Health Organization FRAX, Orthopedics, 35:798-802.
6. **Rosen C, Klibanski A (2009):** Bone, fat, and body composition: evolving concepts in the pathogenesis of osteoporosis. Am J Med., 122:409–414.
7. **Shepherd J (2013):** Is osteoporosis an obesity paradox? J Clin Densitom., 16:131–132.
8. **Salamat M, Salamat A, Janghorbani M (2016):** Association between Obesity and Bone Mineral Density by Gender and Menopausal Status. Endocrinol Metab (Seoul), 31(4):547-558.
9. **Taes Y, Lapauw B, Vanbillemont G *et al.* (2009):** Fat mass is negatively associated with cortical bone size in young healthy male siblings. J Clin Endocrinol Metab., 94:2325–2331.
10. **Chang C, Chang Y, Wang M *et al.* (2013):** Inverse relationship between central obesity and osteoporosis in osteoporotic drug naive elderly females: the Tianliao Old People (TOP) Study. J Clin Densitom., 16:204–211.
11. **Blackburn B, Henry G, Jacobs S *et al.* (2014):** Commentary: Origins and evolution of body mass index (BMI): continuing saga. International Journal of Epidemiology, 43(3): 665–669.
12. **Dohnal L, Kalousová M, Zima T (2010):** Comparison of Three Methods for Determination of Glucose. Prague Medical Report, 111(1): 42–54.
13. **Yang L, Fan B, Yang K *et al.* (2012):** A simple and sensitive method for lipoprotein and lipids profiles analysis of individual micro-liter scale serum samples. Chem Phys Lipids, 165(2):133-41
14. **Uhlin H, Fernström A, LumanM *et al.* (2015):** An optical method for serum calcium and phosphorus level assessment during hemodialysis. Toxins (Basel), 7(3): 719–727.
15. **Revet I, Boesten L, Linthorst J *et al.* (2016):** Misleading FT4 measurement: Assay-dependent antibody interference. Biochem Med (Zagreb), 26(3): 436–443.
16. **Cui L, Shin M, Kweon S *et al.* (2007):** Relative contribution of body composition to bone mineral density at different sites in men and women of South Korea. J Bone Miner Metab., 25:165–171.
17. **Janicka A, Wren T, Sanchez M *et al.* (2007):** Fat mass is not beneficial to bone in adolescents and young adults. J Clin Endocrinol Metab., 92:143– 147.
18. **Zhao L, Liu Y, Liu P Y *et al.* (2007):** Relationship of obesity with osteoporosis. J Clin Endocrinol Metab., 92(5): 1640–1646.
19. **Kim Y, Kim S, Yoo J *et al.* (2016):** Variations in fat mass contribution to bone mineral density by gender, age, and body mass index: the Korea National Health and Nutrition Examination Survey (KNHANES) 2008-2011. Osteoporos Int., 27(8):2543-54.
20. **Sue A, Pop L, Wang Y (2017):** Obesity is a concern for bone health with aging. Nutr Res., 39: 1–13.
21. **Savvidis C, Tournis S, Dede A (2018):** Obesity and bone metabolism. Hormones, 17: 205–217.
22. **Lekamwasam S, Weerarathna T, Rodrigo M *et al.* (2009):** Association between bone mineral density, lean mass, and fat mass among healthy middle-aged premenopausal women: a cross-sectional study in southern Sri Lanka. J Bone Miner Metab., 27:83–88.
23. **Kim J, Kwon H, Heo B *et al.* (2018):**The Association between fat mass, lean mass and bone mineral density in premenopausal women in Korea: A Cross-Sectional Study. Korean J Fam Med., 39(2): 74–84.
24. **Kim C, Oh K, Rhee E *et al.* (2009):** Relationship between body composition and bone mineral density (BMD) in perimenopausal Korean women. Clin Endocrinol (Oxf), 71(1):18-26.
25. **Kim J, Choi H, Kim M *et al.* (2012):** Fat mass is negatively associated with bone mineral content in Koreans. Osteoporos Int., 23:2009–2016.
26. **Campos R, de Piano A, da Silva P *et al.* (2012):** The role of pro/anti-inflammatory adipokines on bone metabolism in NAFLD obese adolescents: effects of long-term interdisciplinary therapy. Endocrine, 42:146–156.
27. **Blum M, Harris S, Must A *et al.* (2003):** Leptin, body composition and bone mineral density in premenopausal women. Calcif Tissue Int., 73:27-32.
28. **Alshafei M, Hanafi E, Saber M *et al.* (2016):** Obesity modulates bone mineral density and hip fracture risk in Egyptian women around menopause. World Appl Sci J., 34 (12): 1869-1875.
29. **Shi Y, Baldock P (2012):** Central and peripheral mechanisms of the NPY system in the regulation of bone and adipose tissue. Bone, 50:430–436.
30. **Douchi T, Yamamoto S, Oki T *et al.* (2000):** Relationship between body fat distribution and bone mineral density in premenopausal Japanese women. Obstet Gynecol., 95:722–725.