ORIGINAL ARTICLE

Relationship of Body Mass Index, Bone Turnover Marker and Bone Mineral Density in Postmenopausal Women

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ABSTRACT:
Objective: To observe the correlation of body mass index (BMI) with bone mineral density(BMD) and bone turnover marker (NTX) in postmenopausal women
Materials and Methods: This observational cross sectional study was carried outfrom January 2014 to December 2014. In this study 85 postmenopausal women were included from Orthopedics and Gynecology outpatient departments of a tertiary care hospital of Karachi.Their BMI in Kg/m^2 and BMD by DEXA scan (femur and lumbar spine) were measured.Seruml evels of bone turn over marker, N-telopeptide of type I collagen (NTX) was assayed by ELISA.To evaluate the relationship between BMI, bone mass and NTX, Pearson Correlation co-efficient was computed (P-value significancewas <0.05).
Results: The correlation between BMI and BMD at both femur(r = 0.060, P = 0.586) and lumbar spine(r =0.093, P=.0.398)was weak and found to be non-significant. The correlation between serum NTX & BMI was negative but also found to be non-significant(r = -0.14, P=0.203).
Conclusion: Both bone mass and bone turnover marker (NTX) are not correlated to an index of obesity, BMI in postmenopausal women in our clinical set up.
Keywords: Bone mass, Body mass index, Obesity, Postmenopausal women, Bone turnover marker.

INTRODUCTION:

Osteoporosis and obesity,both diseases are highly rampant in the global scenario and even more prevalent among women of postmenopausal age group.[1,2]Globally according to an estimate about more than 200 million women have been suffering from osteoporosis. Furthermore, it has been predicted that yearly incidence rate of hip fractures, which is currently 1.66 million would increase to 6.26 million at the end of year 2050.[3]In 2014 WHO reported that worldwide about 1.9 billion of adult population was overweight, out of which more than 600 million were obese. Gender categorization revealed that about 11% of men and 15% of women were obese while 38% of men and 40% of women were overweight, which is clearly showing female predominance in both groups. Across the world, obesity claims 2.8 million lives every year due to its related co-morbidities[4].

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Received: 02-10-2015
Revised: 01-11-2015
Accepted: 03-11-2015

In Pakistan obesity and osteoporosis/ osteopenia (low bone mass) are quite prevalent among postmenopausal populationas documented by multiple studies**.**Qureshi in 2011 reported 63.64% and 30.30% postmenopausal women had osteopenia and osteoporosis respectively, based on BMD measurements by DEXA scan[5]. A study has documented that majority (64.3%) of the women 55 years or older had osteoporosis, which was even more (55.7%) prevalent in obese women[6.] Another study conducted in a tertiary hospital of Karachi showed 89% of postmenopausal women to be obese on the basis of BMI calculation[7]. To measure the extent of obesity, body mass index (BMI) is frequently used, whichis a ratio of weight in kilograms (Kg.) and height expressed in meters square (m^2). For Asians the appropriate BMI values based on WHO proposed cut-offs are from 18.5 to 22.9(kg/m^2).[8]According to WHO criteria the diagnosis of osteoporosis is based on the bone mineral density (BMD), expressed in T-score with a cut off value of -2.5 or more standard deviation (SD) lower than normal reference values[9].

The pathogenesis of osteoporosis and obesityrevolve around avariety of genetic and environmental factors; some of which are common to both of the diseases.Previously it was reported that obesity is positively correlated with increased bone mass[10,11],while some recent researches have regarded obesity as a risk factor forlow bone mass and osteoporosis[12,13,14].Due to theseconflicting results from the previous studiesthemechanisms involved in the common pathogenesis of obesity and bone mass are still not very clear.BMD measured by DEXA scan is the gold standard for the estimation of bone mass but it fails to elicit the changes in bone mass at a particular point of time. While bone markers although considered as surrogate markers for BMD but being dynamic represent the metabolic status of bone mass at any point of time[15].

It has been mentioned that about 90% of organic matrix of bone comprises of type 1 collagen, which being a

helical protein is cross-linked at its two poles,amide(N-terminal) and Carboxyl (C-terminal).Several studies have mentioned that the measurementof level of N-terminal of cross link Telopeptide of type 1 collagen (NTX) is proved to be a useful marker to exhibit elevated bone resorption in clinical conditions associated with increased bone turnover such as osteoporosis and bone metastasis[16,17].Furthermore, NTX is also employed to monitor the treatment response of anti-resorptives in osteoporosis[18]. Keeping in view the significance ofNTX as a marker of bone resorption,we included aforementioned in our current study to further know the exact status of bone at that time.The rationale of our study was to elaborate the correlation between two metabolic conditions,obesity and low bone mass(osteopenia and osteoporosis) by correlating BMD,bone turnover marker NTX and an index of obesity BMI in postmenopausal women in our clinical setup, which was previously not explained only by bone mass or BMD.

MATERIALS AND METHODS:

In this observational cross sectional study 85 postmenopausal women (menopause for six or more than six months) were included in our study by purposive convenient sampling techniquefrom the Orthopedics and Gynaecology OPDs of a tertiary care hospital of Karachi from January 2014 to December 2014. Before inclusion, the patients were explained about the study and their written informed consents were taken for their participation. Patients currently using medications that could affect bone or lipid metabolism were excluded from the study.Their bone densities were measured by DEXA scan (Hologic instrumentation) at lumbar spine and femoral neck. Reference levels were taken according to WHO criteria(T-scores at lumbar spine and femoral neck +1 or more than +1 is normal while -2 to -2.5 is osteopenic and <-2.5osteoporotic)The weight and height of all of the patients were measured in Kg and m^2respectively and after taking their ratios, BMI were calculated.About 4ml of blood was taken from each patient by standard venipuncture technique. Serum was separated after centrifugation, stored at -70$^?$C and assessed collectively at the end of total sample collection.Estimation of the serum levels of N-telopeptide of type I collagen (NTx)(Osteomark, Ostex International, Seattle, WA, USA,LOT no.10049115,REF. no.9021)was done by ELISA at Ziauddin Hospital North Nazimabad. Reference ranges were taken according to the manufacturer's kit (normal cutoffs = 6.2-19 nmol BCE/L(Bone Collagen Equivalent per liter).

Statistical Analysis:

Data was analyzed by Statistical Package for Social Sciences (SPSS) version 17.Quantitative data that is T-score femur neck, T-score lumbar spine,BMI, Serum NTX, duration of menopause(years)and Age (years) were presented in term of Mean SD.To evaluate the relationship between T-score femur neck, T-score lumbar spine,BMI, and Serum NTX, Pearson Correlation coefficient was computed (at level of significance = 0.05). Scatter Plots were used to represent the relationships between variables graphically.

RESULTS:

Table 1 shows the mean SD of the different variables of our study sample.Most of the women were in 51-60 year of ages and their mean duration of menopause was 13.987.39 years. Table 2 shows the frequencyof different classes of BMI, according to WHOin our study subjects.The correlationsof BMI with T-scores of femurneck(r = 0.060, P=0.586) & T-scoresof lumbar spine(r =0.093, P=0.398), both were weak and non-significant.A negative correlation (-0.14, P=0.203) was observed between serum NTX & BMI as shown in Table 3. Figure Ia and Ib shows the pattern of slightly increasing values of BMI corresponding to increasing values of T-score of lumbar spine and femur neck respectively in a linear fashion. In figure I c, all points are quite far from each other but also showing that as the BMI increases, serum NTX decreases which points towards a weak negative association between BMI & serum NTX as shown in Table 3.

Table: 1
Descriptive statistics

Variables	N	Minimum	Maximum	Mean	STD. Deviation
Age (years)	85	40	75	59.88	± 7.867
years since menopause	85	2	30	13.988	± 7.390
BMI	85	17	39	27.55	± 3.944
BMD lumbar spine (T-score)	85	-4	3	-2.47	± 0.733
BMD femur neck (T-score)	85	-4	3	-2.50	± 0.677
Serum NTX nm/BCE	85	21	48	31.70	± 6.818

Table: 2
Classes of BMI and their frequencies (n=85)

CLASSES OF BMI (According to WHO cut off values for Asians)	BMI FREQUENCY Total n=85
Underweight<18	1(1.17 %)
Normal BMI(18-22.9)	10(11.76%)
Over weight(23-24.9)	11(12.94%)
obese>25	63(74.11%)

Table: 3
Correlation between variables

Variables		Correlation (r)	P-Value
BMD femur neck (T-score)	BMI	0.060	0.586
BMD lumbar spine (T-score)	BMI	0.093	0.398
Serum NTX	BMI	-0.140	0.203

P-value significant<0.05

Figure: 1a
Scatter Plot between BMI & T- score Lumbar Spine

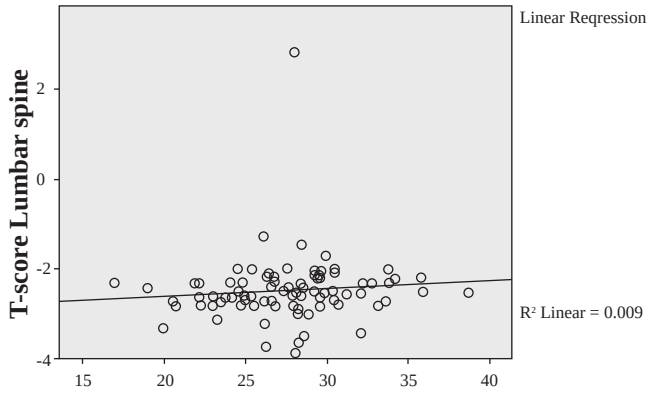


Figure: 1b
Scatter Plot between BMI & T-score Lumbar Spine

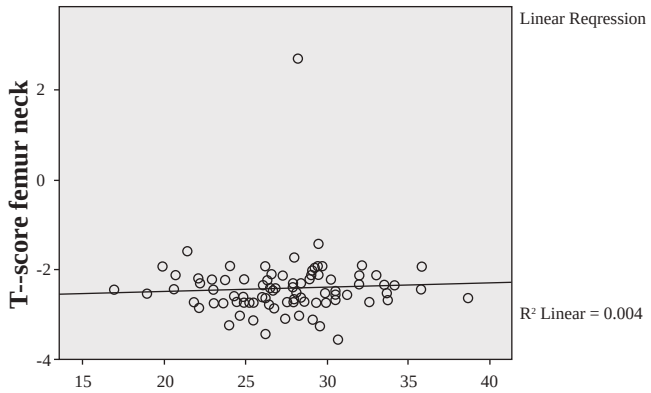
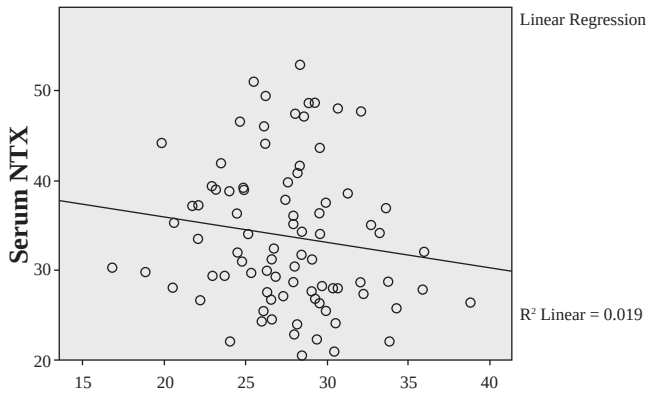


Figure 1c
Scatter Plot between BMI & Serum NTX



DISCUSSION:

In our study, majority of the patients were either obese or over weight (Table 2)which suggests that in our population obesity and its risk factors are highly prevalent in postmenopausal age group. These results are consistent with Khokhar[19]and Begum.[20]The mean BMD of femur neck and lumbar spine in T-scores were found to be lower than cut-offs (Table 1)which showed that the majority of our patients had either osteopenia or osteoporosis.This is strongly supported by previous studies showing osteoporosis and osteopenia most prevalent in postmenopausal women.[21,22.] The mean Serum NTX (nmol BCE/L)of our study group was 31.70 ± 6.818, displaying high bone turnover.This result is also consistent with I wamoto and Sambrook etal.[23, 24] It was reported by a number of studies that greater BMI is related to greater bone mass and weight reduction may cause reduction in bone mass.[11,25]On the other hand some studies have illustrated a converse relation between these two as reported by Hsu et al.that the greater amount of adipose tissue did not reduce the risk of fractures.[26]On the basis of these conflicting results from previous studies, as well as the complexity and involvement of multiple underlying mechanisms the exact correlation between obesity and bone mass is still not convincing. As mentioned earlier,obesity and osteopenia/osteoporosi-shas been detected simultaneously in the postmenopausal women.[1,2]In the current research beside bone density,serum levels of bone turnover marker NTX was also employed to observe their correlation with marker of obesity, BMI in postmenopausal women. Our study results showed that the correlation between BMI and BMD in T-score at both femur(r = 0.060, P = 0.586) and lumbar spine(r =0.093, P=.0.398) were non-significant.These results are in contrast to previous studies which mentioned BMI had positive correlations with BMD.[27, 28]On the other hand Blum et al. documented a negative correlation between proportion of fat and bone mass in 153 premenopausal women.[29] Although a negative correlation (-0.14) was observed between serum NTX & BMI but that was non-significant, P=0.203. It is important to note that all three variables namely,BMD at both femur neck and lumbar spine and serum NTX were not statistically significant when they were correlated with BMI, P=0.586,P=0.398,P=0.203 respectively. Parallel results were displayed by Shaarawy has documented another biomarker of obesity; serum leptin levels to have no correlation with bone turnover markers[30].Contrary to our results, Reid related obesity with BMD, bone markers and increased probability of fractures and in his previous study had already displayed a direct link between BMD and fat mass (P <0.0001)[31]. Our results also differ from Zhao who has displayed a significant negative correlation between BMDand fat mass[14].

In the light of above, it is obvious that high body mass index may not be a risk factor for low bone mass in postmenopausal age group in our community.

CONCLUSION:

Both bone mass and bone turnover marker (NTX) are not correlated to an index of obesity, BMI in postmenopausal women in our clinical set up. However, as learnt from the past studies certain common factors are involved in the development of obesity and low bone mass but a valid pathogenic link is missing between these two metabolic conditions. Further studies with other markers of obesity and bone metabolism in a larger sample size are vital to detect the exact common link between obesity and low bone mass.

ACKNOWLEDGEMENT:
I am gratified to Ziauddin University for the provision of funds required for this project. I am also highly grateful to the laboratory staff of Department of Clinical Biochemistry Ziauddin University and National Medical Centre Karachi for their support in the sample collection and processing.

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