Evaluation of bone mineral density in premature ovarian failure

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Abstract

This study was performed *to evaluate* whether or not early menopause and premature ovarian failure can cause an increased risk of osteoporosis. *The bone mineral density* (BMD) of the 2nd and 4th lumbar spine as well as femoral neck in 29 cases with secondary amenorrhea were compared with a reference data using a dual-energy X-ray absorptiometry on a bone densitometer: Serum levels of luteinizing hormone, follicular stimulating hormone, calcium and phosphorus were also measured. *Both in 20-29 years* and in 30-39 years, BMD were significantly lower than their normal range as compared with a reference data from a large study of the same population (P value<0.05). At lumbar vertebrae, 2 cases had osteopenia and 17 had osteoporosis while at the femoral neck, 17 cases had osteopenia and 4 osteoporosis. Only serum levels of phosphorus had positive relationship with femoral neck BMD (P value<0.05). It may be possible to decrease fracture incidence through the early diagnosis of individuals at risk by BMD. *In conclusion*, our study indicates that females with early onset of menopause and premature ovarian failure had lower value of BMD in both femoral neck and lumbar vertebrae implying the need for more bone health measures.

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Introduction

We would like to evaluate whether early menopause and premature ovarian failure (POF) judged by the levels of estrogens [1] are an increased risk for osteoporosis as estimated by bone mineral density (BMD) values. Bone density starts to decline before normal menopause, is accelerated with the hypoesterogenic conditions [2-6] and after menopause declines progressively for 5-10 years with rates about 3%-1% per year [7, 8]. Although most researchers report that POF induces reduction of bone mass [5] some report no decrease in bone density [9-11].

Subjects and methods

We have studied with BMD prospectively 29 women with secondary amenorrhea before the age of 40 years, at least six months after the last menstruation and with serum follicular stimulating hormone (FSH) levels above 40 UI/L. Our POF patients were 28.7±6 years old, with BMI: 24.9±6.8 kg/m^2, mean time since diagnosis of POF was 4.6±4.2 years.

Cases with a history of smoking more than two cigarettes per day, body mass index (BMI)≥30 or ≤17, fracture or any hip or bone disease, using medication or diet effective on bone mass were excluded. Pregnancy, professional sport, immobility, alcohol and any contrast enhanced radiography taken in the previous 10 days was also considerated as exclusion criteria.

The BMD of lumbar vertebrae (L2-L4) and the neck of proximal femur were measured based on gr/cm^2-using dual-energy X-ray absorptiometery (DXA) on a Hologic bone densinometer (QDR 1000, USA). Precision errors were calculated using the root mean square method. The variation coefficient of the lumbar spine and femoral neck measurements were 0.7% and 0.9% respectively. Quality control test was carried out using the specific phantom of determined density daily before each measurement. According to the WHO criteria , a T score between -1 and -2.5 is indicative of osteopenia, while a T score < -2.5 reflects osteoporosis [12].

Luteinizing hormone (LH) serum levels of calcium, phosphorus and FSH are shown in Table 1. Individuals were categorized in 2 age groups: 20-29 years (71 subjects) and 30-39 years (142 subjects) and bone density of each was compared with the matched age in the normal population, according to the study of the Endocrinology and Metabolism Research Center of Tehran University of Medical Sciences in 2004-2005 [13].

To implement comparison of our BMD values with reference data, the conversion formula was applied [14]. The study complied with the declaration of Helsinki and was approved by the Institutional Ethics Committee of Shaheed Beheshti University of Medical Science and all patients gave written informed consent.

Results

The mean value of BMD in our study was 0.94 ± 0.2 gr/cm^2 in lumbar vertebra and 0.73 ± 0.11 gr/cm^2 in femoral neck. Both were significantly lower than their normal range (Table 1, P<0.01). At lumbar vertebrae, 2 cases had osteopenia and 17 had osteoporosis while in femoral neck, 17 cases had osteopenia and 4 had osteoporosis (Table 2). There was no significant relationship among chronologic age, time from onset of menstruation and the age at menopause with BMD values neither in femoral neck nor in lumbar vertebrae (P value >0.05), but a significant correlation was noted between BMI and BMD values of both femoral neck and lumbar vertebrae (P<0.01). Among biochemical factors, only serum levels of phosphorus had positive relationship with BMD of the femoral neck (Table 3, P<0.05).

Table 1. *Comparison of bone mineral density in premature ovarian failure (POF) and normal population*

BMD (gr/cm2)	Age: 30-39 years			Age: 20-29 years		
	Based on reference data according to Larigani et al [13]	POF	P value	Based on reference data according to Larigani et al [13]	POF	Pvalue
Lumbar vertebrae	1.07±0.08	0.97±0.26	0.01	1.05±0.07	0.93±0.12	0.01
Femoral neck	0.84±0.08	0.72±0.14	0.01	0.79±0.10	0.74±0.07	0.01

Discussion

We observed that BMD of lumbar spine and femoral neck in early onset menopause women was significantly lower than in normal population as matched by age and sex. Individual investigations of BMD information defined that in 13 cases (44%) with POF, the femoral neck BMD was lower than 0.77 g/cm2, which is a risk factor for bone fracture [3]. Others have reported in women with POF that the mean BMD they measured was 1.22 and 0.92 g/cm^2 at the lumbar spine and at the femur respectively, which is significantly lower to the mean of the control group [15]. They noted that age was directly associated with bone density of the spine, whereas BMI and reproductive age were correlated with bone density of the femur [15].

Table 2. *T-score comparison between normal population and premature ovarian failure (POF) group in femoral neck lumbar vertebrae bone mineral density*

t-score		< -2.5		-1 to -2		-1<	
		femoral	vertebrae	femoral	vertebrae	femoral	vertebrae
Age: 20-29 years	POF	6.6%	6.6%	66%	60%	27.4%	33.3%
	Based on reference data according to Larigani et al [13]	2.2%	0%	17.4%	13%	81.4%	87%
Age: 30-39 years	POF	20%	6.6%	50%	50%	30%	43.3%
	Based on reference data according to Larigani et al [13]	0.9%	0%	8.3%	13.9%	91.8%	81.6%

We found a significant association of BMI and BMD in both femoral neck and lumbar vertebrae (P<0.01); however the reproductive age revealed no noticeable correlation with BMD. Others investigating hip and spinal bone mineral density in forty-five women with karyotypically normal spontaneous POF, demonstrated that women with premature ovarian failure had lower BMD than the control group [16]. While other studies have detected that serum levels of E2, LH and FSH were lower in early onset menopause [17], we found only a positive relationship between serum levels of phosphorous with BMD, but there was no significant correlation between BMD and serum level of Ca, FSH and LH. Our results regarding the relationship between BMI and BMD are consistent with our previous studies [18, 19] as well as the study of others where the prevalence of osteoporosis was described to be lower in the group [15, 20].

Table 3. *Mean value of serum level of FSH, LH, Ca, and phosphorus in patients involved in the study*

Parameter	Value
FSH(IU/mL)	60.56±60.14
LH (IU/mL)	23±12.5
Calcium (mg/dL)	9.8±1.2
Phosphorus (mg/dL)	3.65±0.76

In conclusion, our study indicates that females with early onset of menopause and premature ovarian failure had a lower value of BMD in both femoral neck and lumbar vertebrae as compared with a reference data from a large study of the same population implying the need for more bone health measures.

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