ISSN: 0975-8585

Research Journal of Pharmaceutical, Biological and Chemical Sciences

Correlation of Proximal Femoral Geometry with Bone Mineral Density and Serum Osteocalcin in Assessing the Risk of Hip Fracture in Postmenopausal Women.

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ABSTRACT

Hip fracture is an outcome of age related osteoporosis. Factors like Proximal femoral geometry, Low bone mineral density are helpful in assessing the risk for hip fracture. Osteocalcin, bone Gla protein a biochemical marker of high bone turnover is also suggested for predicting the risk for hip fracture. Proximal femoral geometry includes measurement of hip axis length (HAL), Neck shaft angle (NSA) and neck width (NW). The purpose of this study is to find the association between proximal femoral geometry, BMD and serum osteocalcin. The subjects under study 60 post-menopausal women and were divided into two groups. Group 1 includes control group (n=30), Women who had normal BMD as per WHO criteria and Group 2 includes fracture risk group (N=30),Women who had osteopenia or osteoporosis as per WHO criteria).For both the groups, age, height, weight, BMI were recorded. Hip axis length, (HAL), neck shaft angle (NSA), neck width and BMD were measured from the DXA (Dual energy X ray Absorptiometry) print out. Blood sample was collected and serum osteocalcin was estimated. Test of significance and bivariate correlation test was done to find the association between the above factors. Bivariate correlation test shows that BMD was negatively correlated with HAL and NSA and serum osteocalcin was positively correlated with HAL, and NSA and the mean value of HAL and NSA were higher in fracture risk group. Collective assessment of proximal femoral geometry with bone mineral density and serum osteocalcin can provide a better picture in the prediction of hip fracture risk than assessing individually so that the occurrence can be prevented at the earliest.

Keywords: proximal femoral bone, mineral density, osteocalcin, hip fracture

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ISSN: 0975-8585

INTRODUCTION

Hip fracture in the elderly population is a severe public health problem and it is a serious condition that has been found to increase the morbidity and mortality in elderly women [1]. Its incidence rises proportionally with age [2].Worldwide, the number of hip fractures has been estimated to rise from 1.7 million in 1990 to 6.26 million by the year 2050.The etiology of hip fracture is multifactorial, and many of the risk factors have been identified [3]. Age, diseases and trauma are the three main causes that play an important role in the etiopathology of hip fractures and post menopausal women are still more prone to fracture, because of hormonal deprivation.

Hip fracture is also an out come of age related osteoporosis [4]. Proximal femoral geometry and factors like age, sex, low body weight, cigarette smoking are suggested for hip fracture risk other than low bone mineral density defined by the National osteoporosis Foundation 1998. The geometry of the proximal femur and its possible correlation with the incidence of hip fractures is analyzed by various workers with Dual energy x- ray absorptiometry(DXA) scan [5-7], as a mean of assessing bone quality by measuring bone mineral density. They emphasize the importance of osteoporosis as a predisposing factor in hip fractures. Some authors focused on hip axis length(HAL), neck shaft angle(NSA) and neck width(NW) as a measure of indicating fracture risk [5-9].

Biochemical markers of bone metabolism are tools of great importance in understanding the pathophysiologic basis for metabolic diseases of the bone. Determination of protein fragments produced by osteoblasts like osteocalcin or enzymes released during osteogenesis such as alkaline phosphatase are commonly used to assess osteoblastic activity, More recently bone turn over markers have been studied for their ability to predict bone loss. Serum osteocalcin which is a bone Gla protein is a valid marker of bone turnover when resorption and formation are coupled and is a specific marker of bone formation when formation and resorption are uncoupled. In this study the status of femoral geometry, Bone mineral density (BMD), and level of osteocalcin in osteoporotic and non osteoporotic post menopausal women and their correlations is analyzed.

MATERIALS AND METHOD

After getting institutional ethical committee clearance and informed consent from the participants, the study subjects were divided into two groups.

They are as follows.

Control group (n=30):

Post-menopausal women who had normal BMD as per WHO criteria (T >-1 SD) were included in this group. i.e., the T score is more than-1)

Fracture risk group (n=30)

Post-menopausal women who had osteopenia (T <-1 SD toT >-2.5) or osteoporosis (T<-2.5 SD) are included in this group. Osteopenia is considered to be present when the value for bone-mineral content is more than one standard deviation but not more than 2.5 standard deviation below the mean for young adults (i.e., the T score is less than -1 and more than -2.5). Osteoporosis is considered to be present when the value is more than 2.5 standard deviation below the mean bone content for young adults (i.e., the T score is less than -2.5). Severe Osteoporosis is considered to be present when the value for bone mineral content is more than 2.5 standard deviation below the mean for young adult.

Exclusion criteria

The patients with hip fracture, any metabolic bone disease, or on treatment with sex hormones, calcitonin or bis-phosonates were excluded from this study.

For both the groups age , BMI, HAL,NSA, NW, and BMD were recorded and measured from their DEXA scan print out. Hip Axis Length was measured as per the definition as distance from the centre of the head of femur to the base of the greater trochanter. Neck Shaft Angle was measured between the axis of the head and neck with the axis of shaft of femur. Neck Width was measured as the shortest length of the neck of femur. Blood samples were collected from all the participants under aseptic precautions. EDTA plasma was the sample for osteocalcin estimation which was separated with the help of refrigerated centrifuge and stored at -20^{O}C.Osteocalcin was estimated by (Bio-Source Europe SA) a solid phase enzyme amplified sensitivity immunoassay (EASIA) using Monoclonal Antibodies detected against distinct epitopes of human osteocalcin. The amount of substrate turnover was determined colourimetrically by measuring the absorbance which is proportional to the human osteocalcin concentration.

Statistical analysis

The data were entered into the SPSS format and student' test was used to compare the mean difference between the variables of control and fracture risk group. The bivariate Pearson correlation test was performed between the variables of controls and fracture risk group to define its relation.

RESULTS

In Group I the mean values of the anthropometric parameters like age , BMI were 50.44yrs and 26.87kg/m^2. The mean values of upper femoral morphometric parameters like HAL,NSA,NW were 10.55cm, 127 degree and 3.74cm. The mean values of BMD and osteocalcin were found to be 0.908g/cm^2 and 11.26ng/ml as shown in Table1 **.**

In Group II the mean values of the anthropometric parameters like Age, BMI were 53.6yrs and 26.87kg/m^2. The mean values of the upper femoral morphometric parameters like HAL, NSA NW were 10.6cm, 128.78^0, 3.76cm. The mean values of BMD and osteocalcin were found to be 0.704g/cm^2 and 16.16ng/ml as shown in table1. The hip axis length, Neck shaft angle and osteocalcin were higher and BMD was found to be low in osteoporotic women.

Table 1: Shows mean standard deviation and test of significance of femoral geometry, BMD and osteocalcin between group1 and Group2.

	GROUP 1	GROUP 2	P value
AGE(years)	50.44±12.1	53.6±12.5	Sig
BMIkg/m2	26.8±4.39	26.7±4.3	NS
HAL(cm)	10.55±.312	10.65 ±.313	Sig
NW(cm)	3.74±.17	3.76±.17	NS
NSA(degree)	127.8±7.4	128.29±7.4	SIg
BMDg/cm2	0.908±0.093	0.704±0.096	SIg
OSTEOCALCIN ng/ml	11.26±3.07	16.16±4.5	SIg

In this study the Pearson' correlation coefficients between anthropometric, upper femoral morphometric BMD, osteocalcin were calculated to evaluate the relationship between the above factors as shown in table 2.

Age had positive correlation with HAL (r = 0.303; p = 0.002), NSA(r=0.282; p=0.003) and negatively correlated BMD (r = - 0.267 p = 0.005).

BMI had positive correlation with BMD (r = 0.339 BMD, p = 0.000).

NW had positive correlation with HAL(r=0.342 p = 0.000).

BMD had negative correlation with age, (r = - 0.267 p = 0.005), HAL(r = - 0.389 ; p = 0.000 and NSA(r = 0.239; p = 0.13).

Serum osteocalcin was positively correlated with age(r=0.303,p=0.002), HAL(r=0.215,p=0005) and NSA(r=0.282,p=.002) and negatively correlated with BMD(r=0.595,p=0.019).

ISSN: 0975-8585

Table 2: Bivariate correlation between femoral geometry, BMD and osteocalcin

	AGE	BMI	HAL	NW	NSA	BMD	OSTEOCALCIN
Age	1	.109	.303**	-.018	.282**	-.267**	0.303
		.264	.002	.851	.003	.005	0.002
	60	60	60	60	60	60	60
BMI	.109	1	-.182	.106	.072	.339**	0.182
	.264		.061	.276	.464	.000	0.061
	60	60	60	60	60	60	60
HAL	.303**	-.182	1	.342**	-.004	-.389**	.215**
	.002	.061		.000	.964	.000	.005
	60	60	60	60	60	60	60
NW	-.018	.106	.342**	1	-.102	-.025	.115
	.851	.276	.000		.298	.801	.305
	60	60	60	60	60	60	60
NSA	-.282**	.072	-.004	-.102	1	.239*	.282**
	.003	.464	.964	.298		.013	.002
	60	60	60	60	60	60	60
BMD	-.267**	.339**	-.389**	-.025	-.239*	1	.595
	.005	.000	.000	.801	.013		0.019
	60	60	60	60	60	60	60
OSTEOCALCIN	.303	.182	.215	.115	.282	.595	1
	.002	.061	.005	.305	.002	.019	
	60	60	60	60	60	60	

** Statistically significant.

DISCUSSION

The high bone turnover can disrupt the trabecular architecture and its deterioration is a contributory factor to the bone fragility, which increases the incidence of trabecular perforation and buckling, thus reducing the bone strength in osteoporosis, ultimately resulting in decreased levels of bone mineral density . A significant negative correlation between BMD and serum osteocalcin was observed in our previous study. Since there exists a relation between bone mass (which is determined by BMD) and bone turn over (which is assessed by the level of serum osteocalcin), the relation of femoral geometry like Hip Axis Length,Neck Shaft Angle, Neck Width were also focused in this present study along with BMD and osteocalcin.

Ageing is also one of the important reasons for osteoporotic related hip fracture. It increases exponentially with age [5]. The individual with shorter height has a lower risk of hip fracture compared to tall individuals [10], though opposite findings have also been reported by Huopio et al in 2000 [11]. An increased risk of hip fracture is observed in individuals who are thin, as low weight accounts for very low bone mass density. Low body weight is generally a marker of poor health that increases the fragility of bone. Regarding geometric factors also, controversial reports are suggested for their association with fracture risk. Some studies showed the relationship between HAL and fracture risk [12-14] and others like Alonso et al., and Pande et al., show no association [5,6]. In a similar manner the relation of neck shaft angle as a risk factor for hip fracture is also debatable. According to Nakamura et al 1994, its value is greater in fracture patients [15] compared with the controls and refuted by others like Faulkner et al., [12]. Mesut tastan considered that neck width in predicting fracture risk of femur [16]. Currently bone mineral density measurement by DXA scan is gold standard in prediction of osteoporotic related hip fracture in post-menopausal women. The work by Ercan Dincel in 2008 also associated proximal femoral geometry with BMD values [17]. In this study an association between BMD and HAL and NSA was noticed consistent with the above study.

Several studies carried out in different societies have found that the incidence of hip fractures differs from country to country. Even though evidence suggests that proximal femoral morphometry, is equally important in determining hip fracture risk certain discrepancies concerning the effect of proximal femoral morphometry on fractures were described by following authors like Hoaglund DeLaet and Schwartz [18-20].These discrepancies may be due to racial differences in proximal femoral morphometry among populations.. The variations in skeletal morphometric measurements are associated with genetic and environmental factors (Geography, diet, life styleetc. India is a large country with a wide variety of

environmental conditions. It shows ethnic multiplicity and is characterized by an interracial mixing rarely seen in other countries. Taking into account of these factors the data base obtained in our study may not be representative of the entire Indian population and there fore our normative data should be used only for a population sharing the same genetic potential and living under similar environmental conditions. One limitation of our study was the recruitment of volunteers. The study sample was not population based but recruited for bone densitometry causing a bias in selecting the subjects. The risk of fracture is dependent on the geometry of the bone, its architecture at all sites of hierarchy, its material properties and the distribution of material properties and the character of the imposed load (magnitude, rate, and direction). Non invasive imaging techniques can provide geometric measurements and also its correlation to macroscopic material properties (BMD). Until effective methods for measuring micro architecture and genetic or other biomarkers for individual response dynamics are available in clinical practice, we have to depend on Proximal Femoral geometry and BMD to predict susceptibility to fracture in patients.

BMD is the best quantifiable predictor of osteoporotic fractures. But the efficacy of the treatment cannot be judged immediately, since the period for structural recovery time of the bone is little longer. Serum osteocalcin being a dynamic marker, the efficacy of the treatment can be assessed by repeating the estimation of osteocalcin and by comparing it with its original value. Thus, the assessment of osteoporotic risk fractures can be done effectively by a combination of BMD, reflecting the static feature of the skeleton and the biochemical marker, osteocalcin, reflecting the dynamic measure of the bone remodeling unit, as was evidenced from the study of Vanitha et al [21].

CONCLUSION

Significant correlation of proximal femoral geometry, BMD and osteocalcin was observed in this study. Collective assessment of proximal femoral geometry with bone mineral density and serum osteocalcin can provide a better picture in the prediction of hip fracture risk than assessing individually so that the occurrence of hip fracture can be prevented at the earliest.

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