

CONCORDANCE OF BONE MINERAL DENSITY (BMD) AND BIOCHEMICAL PARAMETERS FOR THE DIAGNOSIS OF OSTEOPOROSIS IN POSTMENOPAUSAL WOMEN STUDIED AT KIRAN, KARACHI, PAKISATAN

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ABSTRACT

Osteoporosis is a skeletal disease characterized by low bone mass and micro architectural deterioration of bone tissue, leading to enhanced bone fragility and a consequent increase in fracture risk. Correlation of bone mineral density (BMD) measured by dual energy X-ray absorptiometry (DEXA) and biochemical parameters (Urinary excretion of calcium, phosphate, zinc and serum estrogen) for the diagnosis of osteoporosis in pre and postmenopausal women of Karachi was carried out.

A total of 90 women including 50 post menopausal and 40 pre menopausal women were selected. There was no history of any drug use for bone loss in both groups. Bone mineral density was measured by DEXA at the lumbar spine (LS BMD) and total hip (H BMD). Biochemical parameters were measured on biochemistry analyzer or on spectrophotometer by using Randox and biosystem kits and serum estrogen was measured by using Enzyme Immunoassay.

Comparison of BMD measured at hip and lumbar spine shows that the BMD at hip was 0.80 ± 0.017 , 1.09 ± 0.026 gm/cm² in post and pre menopausal women respectively which is significantly low in post menopausal subjects ($P < 0.001$). Similarly BMD at lumbar spine shows 0.75 ± 0.017 , 0.94 ± 0.016 gm/cm² in post and pre menopausal women respectively which is also significantly low in post menopausal women ($P < 0.001$). Distribution of postmenopausal women into normal, osteopenic and osteoporotic according to the finding of BMD measured at hip and spine depicts that out of 50 post menopausal women, only 4 (8%) were normal, where as 22 women (44%) were osteoporotic and remaining 24 (48%) were osteopenic.

Biochemical parameters show that the mean urinary calcium, phosphate and zinc was significantly higher ($P < 0.001$) where as estrogen was found to be significantly decreased in postmenopausal women.

Key-words: Osteoporosis, skeleton disease, Bone Mineral Density, Post-menopausal women, Karachi, Pakistan.

INTRODUCTION

Osteoporosis is a common condition affecting one in three women and one in 12 men, resulting in a substantial morbidity, excess mortality and health and social services expenditure (Nelson *et al* 2002). The WHO definition of osteoporosis is based on measurement of bone mineral density (BMD) of >2.5 standard deviations (SD) below the mean for young adults, while osteopenia is defined as a BMD between 1 and 2.5 SDs below the means for young adults (T score) (Eastell, 1998) (WHO report 1994). The risk of fracture increases to three fold for each SD decrease in BMD (Marshall *et al.*, 1996). The disease is common in postmenopausal women (Melton *et al.*, 1990) however; the disease prevalence varies in different population. Umer *et al.*, (2003) reported the prevalence of osteoporosis 8.7% and osteopenia 22.5% in postmenopausal in Mayo hospital Lahore. In another mega study 40% postmenopausal osteopenia and 7% osteoporosis was found by peripheral bone densitometry (Siris *et al* 2001). It is widely accepted that BMD measurement measured by DEXA is the gold standard of diagnosis of osteoporosis (Siris *et al* 2001; Lewiecki, 2004; Grampp *et al* 1999). A study conducted by Habiba *et al* (2002) at Hayatabad medical complex, Peshawar in 1997-98 on thousand postmenopausal women for simple calculated osteoporosis risk estimation, found that 75.3% were predisposed to osteoporosis and the risk increased with age (97% in women of 75-84 years of age compared to 55% in women of 45-54 years of age).

Bone markers could be used for early diagnosis of bone metabolic diseases. Biochemical markers of bone resorption that reflect osteoclast activity and/or collagen degradation provide a new and potentially important clinical tool for the assessment and monitoring of bone metabolism (Christenson, 1997; Garnero *et al.*, 1996). Most of the new biochemical markers have been targeted for use in assessing bone resorption, since bone loss due to metabolic bone disease is the more important clinical factor to monitor and evaluate in bone disease patients (Demers, 1997). Metabolic products of bone collagen breakdown have been the recent focus of laboratory methods design to assess bone resorption (Demers, 1997). Products of bone breakdown include calcium and bone matrix degradation products such as hydroxylysine glycosides, collagen pyridinium, cross-links, cross linked telopeptides and hydroxyproline (Demers, 1997).

These bone turnover markers may be measured in serum and urine. The effect of estrogen on bone remodeling is to decrease activation frequency and subsequent decrease in numbers of osteoclasts and osteoblasts (Eastell, 2005).

According to our knowledge, not much work has been done on osteoporosis in particular on biochemical markers and BMD. The objective of the study was to find out correlation of bone mineral density (BMD) measured by latest technique of dual energy X-ray absorptiometry (DEXA) and biochemical parameters (Urinary excretion of calcium, phosphate, zinc and estrogen) for the diagnosis of osteoporosis in pre and postmenopausal women of Karachi.

MATERIALS AND METHODS

PATIENTS:

A total of 90 women including 50 post menopausal and 40 pre menopausal women were selected. There was no history of any drug use for bone loss in both groups

BIOCHEMICAL TESTS:

Biochemical parameters (Twenty-four hour urinary, calcium, phosphate, and zinc) were measured on biochemistry analyzer or on spectrophotometer by using Randox and biosystem kits as per supplier's instructions. Serum estrogen was measured by using Enzyme Immunoassay kit EIA-2693 as per supplier instructions in pre and postmenopausal women.

DEXA:

Bone mineral density was measured by latest technique of DEXA. BMD was measured by DXA with a QDR (Quantitative Digital Radiography) Discovery device (Hologic, Waltham, MA, USA) at the lumbar spine (LS BMD) and total hip (H BMD). The WHO definition of osteoporosis is based on measurement of bone mineral density (BMD) of >2.5 standard deviations (SD) below the mean for young adults, while osteopenia is defined as a BMD between 1 and 2.5 SDs below the means for young adults the gold standard of diagnosis of osteoporosis (Siris *et al* 2001; Lewiecki *et al* 2004; Grampp *et al* 1999).

RESULTS

Comparison of biochemical parameters in pre and postmenopausal women show that the mean urinary calcium, phosphate and zinc was significantly higher ($P<0.001$) where as estrogen was found to be significantly decreased in postmenopausal women, moreover, urinary creatinine was non significant among pre and postmenopausal women (Table 1).

Table 1. Comparison of biochemical parameters.

	Biochemical Parameters	Premenopausal (n=40)	Postmenopausal (n=50)	Osteopenic (n=24)	Osteoporotic (n=22)
1	Urinary calcium (mg/g creatinine)	126.12 \pm 4.975	216.80 \pm 11.24*	163.87 \pm 8.23	292.63 \pm 8.61*
2	Urinary phosphate (mg/g creatinine)	463.08 \pm 11.493	527.20 \pm 18.02*	447.71 \pm 13.68	641.38 \pm 18.63*
3	Urinary zinc (μ g/gm creatinine)	488.53 \pm 24.69	710.93 \pm 29.03*	607.17 \pm 33.57	865.80 \pm 30.36*
4	Urinary creatinine (g/24 hours)	1.045 \pm 0.012	1.078 \pm 0.011 ^{NS}	1.07 \pm 0.017	1.07 \pm 0.018 ^{NS}
5	Serum estrogen (pg/ml)	106.41 \pm 6.69	45.082 \pm 3.44*	48.96 \pm 6.84	40.50 \pm 2.17*

* $P<0.001$ statistically significant as compared to pre menopausal group, NS: Non- significant.

Similarly, mean urinary calcium, phosphate and zinc was significantly higher ($P<0.001$) where as estrogen was found to be significantly decreased in osteoporotic compared to osteopenic women, moreover, urinary creatinine was non significant among pre and postmenopausal women (Table 1).

Comparison of BMD measured at hip and lumbar spine in pre and post menopausal shows that the BMD at hip was 0.80 ± 0.017 , 1.09 ± 0.026 gm/cm² in post and pre menopausal women respectively which is significantly low in post menopausal subjects ($P<0.001$). Similarly BMD at lumbar spine shows 0.75 ± 0.017 , 0.94 ± 0.016 gm/cm² in post

and pre menopausal women respectively which is also significantly low in post menopausal women ($P < 0.001$) (Table 2). Distribution of postmenopausal women into normal, osteopenic and osteoporotic according to the finding of BMD measured at hip and spine depicts that out of 50 post menopausal women, only 4 (8%) were normal, where as 22 women (44%) were osteoporotic and remaining 24 (48%) were osteopenic (Table 4). Similarly, comparison of BMD at hip and lumber spine shows a significant difference in osteoporotic and osteopenic women ($P < 0.001$) (Table 2).

Table 2. Comparison of bone mineral density masured at hip and lumber spine.

	Bone mineral density	Premenopausal (n = 40)	Postmenopausal (n = 50)	Osteopenic (n = 24)	Osteoporotic (n = 22)
1	Bone mineral density at hip (g/cm^2)	$1.09.62 \pm 0.026$	$0.80. \pm 0.017^*$	0.878 ± 0.017	$0.703 \pm 0.014^*$
2	Bone mineral density at lumber spine (g/cm^2)	0.94 ± 0.016	$0.75 \pm 0.0.017^*$	0.857 ± 0.015	$0.684 \pm 0.0.017^*$

* $P < 0.001$ statistically significant.

Table3. Correlation coefficient of biochemical parameters with bone mineral density.

S.NO	Biochemical parameters	OSTEOPENIC POSTMENOPAUSAL WOMEN		OSTEOPOROTIC POSTMENOPAUSAL WOMEN	
		at hip	at lumber spine	at hip	at lumber spine
1	Urinary calcium (mg/g creatinine)	-0.6**	-0.5*	-0.58*	-0.07
2	Urinary phosphate (mg/g creatinine)	-0.5*	-0.4	-0.65**	-0.13
3	Urinary zinc ($\mu\text{g}/\text{g}$ creatinine)	-0.12	-0.25	-0.19	-0.51*
4	Urinary creatinine ($\text{g}/24$ hours)	-0.09	0.13	-0.18	0.14
5	Serum estrogen (pg/ml)	0.07	-0.05	0.04	-0.04

* $P < 0.05$, ** $P < 0.01$

Mean age of postmenopausal osteopenic women was significantly higher (59.18 ± 1.64) than osteoporotic (54.38 ± 1.69) postmenopausal women ($P < 0.05$).

Urinary calcium shows strong negative correlation with BMD at hip ($r = -0.6$) and moderate correlation at lumber spine ($r = -0.5$) in osteopenic postmenopausal women ($P < 0.001$) Similarly, urinary phosphate shows moderate negative correlation with BMD at hip ($r = -0.5$) but poorly correlated at lumber spine ($r = -0.4$) where as other biochemical parameters show poor correlation with BMD both at hip and lumber spines (Table 3).

Urinary calcium shows moderate correlation with BMD at hip ($r = -0.58$) and poor correlation at lumber spine ($r = -0.07$) in osteoporotic postmenopausal women ($P < 0.001$) Similarly, urinary phosphate shows strong negative correlation with BMD at hip ($r = -0.65$) but poorly correlated at lumber spine ($r = -0.13$) where as other biochemical parameters show poor correlation with BMD both at hip and lumber spines (Table 3).

DISCUSSION

Many studies have been conducted in the world to highlight changes in BMD with progression of female age. It has long been known that at least 50% of osteoporotic and osteopenic women are likely to develop a spontaneous fracture in later life as a result of post menopausal osteoporosis. It is not just age which brings rapid bone loss after menopause but biochemical changes a woman undergoes after her reproductive age exert its toll on bone density.

Considering above facts this study was planned in Karachi among 90 urban women with 40 pre- and 50 postmenopausal women. Apart from age there was no significant difference in other physical parameters like height,

weight and BMI in pre and postmenopausal women. However, significant difference was observed with respect to biochemical parameters in both groups. Comparison of biochemical parameters in pre and postmenopausal women show that the mean urinary calcium, phosphate and zinc was significantly higher in postmenopausal women which is consistent with the earlier work of George (2003) who also showed that during bone loss calcium, and phosphate are released from bone and hence considered as an index of bone resorption and a major determinant of bone status. Skeleton is a major reservoir of calcium and phosphate as 58-90% of body calcium and phosphate are found in skeleton. Higher urinary calcium and phosphate levels in postmenopausal women as shown in this study confirm the earlier findings of Delmas (1993) that 90% of these substances released by the breakdown of collagen in tissues especially during bone resorption. Similarly hyperzincuria in postmenopausal women as shown in our results is also reported earlier by Herzberg *et al.*, (1990) according to him half of body zinc is present in skeleton and during bone loss zinc escapes from bones together with other minerals and collagen degradation products. The values of biochemical parameters are expressed in relation to creatinine in this study because creatinine is excreted in urine in relatively constant amount proportional to the individual muscle mass, thus serving as a reference standard (George, 2003). Twenty four hours urinary creatinine signifies the renal function and was observed within normal limits in our study in both pre and postmenopausal subjects.

The BMD of premenopausal women analyzed by DEXA and none showed osteopenia or osteoporosis which is also reported earlier (Gambacciani *et al.*, 1993; Cooper *et al.*, 1995).

The BMD at hip and lumbar spine of 46 out of 50 postmenopausal women by DEXA showed low and only 4 had normal BMD. Out of these 46 women with low BMD, 22 were osteoporotic and 24 were osteopenic. This shows that BMD decreases markedly after menopause. Similar findings are reported by Hayashi (2004) and Garnero *et al.*, (1996).

Higher values were observed in urinary excretion of biochemical parameters (Calcium, phosphate and zinc) and serum estrogen in all osteoporotic women, these findings are consistent with earlier work of Herzberg *et al.*, (1990) and Schneider *et al.*, (1997). Study of BMD in osteopenic and osteoporotic women shows a decline of BMD at hip and lumbar spine in osteoporotic subjects which is in line with earlier work of Garnero *et al.*, (1996).

We found a significant inverse correlation of urinary calcium and phosphate with BMD in osteopenic and osteoporotic subjects, this is due to the fact that menopause is associated with increase in urinary excretion of calcium and phosphate with a decrease in their absorption. Less calcium absorption in the postmenopausal women increases parathyroid hormone activity which contributes increased rate of bone resorption and loss of bone mass (Inman *et al.*, 1999). On the other hand our results depicts that urinary zinc shows inverse correlation with BMD at lumbar spine in osteoporotic women, Herzberg *et al.*, (1996) also showed that elevated zinc excretion is a feature of established osteoporosis in elderly women and reflects the accelerated bone resorption process occurring in osteoporosis in postmenopausal women. Study of serum estrogen levels in osteopenic and osteoporotic women reveals that a direct correlation exist between estrogen with BMD, same findings reported by Cauley *et al.*, (2001) while Quigley *et al.*, (1987) demonstrated that initiating estrogen therapy in postmenopausal women was associated with increased BMD and hence protected these women from becoming osteoporotic.

Present study reveals that there is an inverse significant association between bone mineral density and urinary excretion of calcium, phosphate, zinc and direct association serum estrogen levels with BMD. Decrease in BMD measured at hip and lumbar spine resulted in corresponding increase in urinary excretion of calcium, phosphate, zinc and decrease in serum estrogen levels in postmenopausal women particularly osteoporotic subjects. It is concluded that BMD is greatly affected by menopause, more the number of years after menopause the less will be BMD, probably, more will be chances of bone fracture.

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