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Biochemical Markers Of Bone Turnover in Egyptian Women at Different Ages

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Abstract:

Osteoporosis is a metabolic bone disease characterized by bone remodeling .This study was done for the detection of some blood and urine markers in cases of osteoporosis among Egyptian women at different ages .The study included 100 women divided into three groups. The first group included 33 women their ages ranged between 35-45 years old, the second included 33 women their ages ranged between 45-55 years old and the third group included 34 women their ages were above 55 years old. Fore all subjects DEXA densitometry was performed. Serum calcium, phosphorous, alkaline phosphatase, Osteocalcin and urinary hydroxyproline, deoxypyridinoline and creatinine were estimated. Results: In osteopenic and osteoporotic women there was elevation in serum alkaline phosphatase and osteocalcin and in urinary pyridinoline and hydroxyproline, while there was decrease in serum calcium .Conclusion: The Egyptian women subjected to the study were suffering from osteopenia from the age of 35 years old or may be earlier Above the age of 55 (postmenopausal) it was found that 50% of women were osteopenic and osteoporotic.

Introduction

Throughout life, bone is formed and resorted (degraded) in a dynamic process called "bone remodeling". Early in life, this process leads to bone growth and ultimately peak bone mass is achieved by 30 to 35 years of age. In contrast, the later years of life are characterized by a shift towards increasing bone resorption, which contributes the risk of fracture and osteoporosis, particularly in postmenopausal women **(Delmas et al., 2009).**

Osteoporosis is a condition in which an imbalance appears between bone resorption and formation, with bone resorption exceeding formation **(Mora, 1999).**

Biochemical markers of bone turnover allow clinicians to evaluate the risk of bone loss and provide insight into response to therapy **(Millar et al., 2008). A National Osteoporosis Foundation Clinian`s guide to the prevention and treatment of osteoporosis (2008)** states that biochemical markers of bone remodeling (resorption and formation) can be measured in the serum and urine in untreated patients to assess risk of fracture. These markers can demonstrate wide variation between patients and within the same patient from day to day and are affected by food intake and time of day, and lack assay standardization, limiting their clinical utility **(North American Menopause Society, 2010).**

Their application should be reserved for individuals at high risk as a way of monitoring therapeutic effect on bone turnover. The bone turnover marker response pattern with denosumab, a human monoclonal antibody to RANkL, is unique and should be appreciated by physicians to monitor this treatment effectively **(Eastell et al., 2011).**

Clinical questions that might be answered by bone markers include diagnosing osteoporosis, identifying fast *bone* losers, and patients at high risk fracture, selecting the best treatment for osteoporosis and providing an early indication of the response to treatment **(Brown et al., 2009).**

The aim of this work was the detection of some blood and urine markers of osteoporosis among Egyptian women at different ages.

Subjects and Methods

The study included 100 women divided into three groups

- The first group: included 33 women, their ages ranged between 35 to 45 years old.
- The second group: included 33 women, their ages ranged between 45 to 55 years old.
- The third group: included 34 women, their ages were above 55 years old.

All individuals were subjected to the following:

1) History and general examination.
2) Investigations included determination of serum calcium **(Gindler and King 1972),** serum inorganic phosphate **(Yee, 1968)**, serum alkaline phosphatase **(Scand, 1974),** osteocalcin in serum **(Delmas, 1993),** urinary deoxypyridinolone **(Rabins, 1994),** urinary creatinine **(Kostir and Sonka, 1952)** and urinary hydroxy proline **(Varley et al., 1980).** Performance of the dual energy x-ray absorptiometry (DEXA) was done according to Pouilles **et al. (1996)** to determine the bone mineral density of vertebrae and femurs.

Result

All women in the three studied groups were subjected to Dual energy x-ray absorptiometry (DEXA). The percentage and T-score of bone mineral density (BMD) were estimated in anteroposterior (AP) spine and left (It.) femur.

According to the obtained results the subjected women were classified into three categories (Table 1)

- Normal women: T-score up to –1.5, osteopenic women: T-score between -1.5 to -2.5 and osteoporotic women: T-score below -1.5.
- In the first group, there were twenty-five normal women, seven osteopenic women and only one osteoporotic woman.
- In the second group, there were twenty-seven normal women and six osteopenic women.
- In the third group, there were seventeen normal women six osteopenic women and eleven osteoporotic women.

Table (1): Percentage (%) of the disease among the three groups

Group	**Normal**		**Osteopenia**		**Osteoporosis**		**P value**	**Total**	
	n =	%	n =	%	n =	%		n =	%
I	25	76 %	7	21%	1	3%	<0.001	33	33%
II	27	82 %	6	18%	0	0%		33	33%
III	17	50 %	6	18%	11	32%		34	34%
Total	69	69 %	19	19%	12	12%		100	100%

For all subjects, biochemical markers for both bone formation and resorption were estimated. Osteocalcin (OC) and alkaline phosphatase (AIP) in serum, the most sensitive markers of bone formation while deoxypyridinoline (Dpd) and hydroxyproline (OHP) in urine were measured as markers of bone resorption. Serum calcium and phosphorous were measured in all groups (Table 2).

The results of the present study revealed significant higher level of OC in the third group (III) when compared to the other groups II&I.

However, when comparing osteoporotic and osteopenic women in each of the three studied groups with normal women, the results obtained indicated significantly higher levels for OC.

The current data indicated the presence of an inverse correlation between OC and BMD.

Table (2): Levels of some investigated parameters among the three groups.

Group	Group 1		Group II		Group III	
Variable	Mean	± SD	Mean	± SD	Mean	± SD
Age	40.76*	3	50.9*	3.1	58.7*	3.9
Ap Spine B.D.%	98.5	13	97.67*	11	89.88*	14.1
Ap Spine B.D. T-score	-0.23	1.3	-0.23*	1	-1.03*	1.4
Lt Femur B.D.%	105.42	14.5	105.2	11.24	100.26	15.3
Lt Femur T-score	0.57	0.2	0.48	0.08	-0.01	1.4
Calcium (mg/dI)	9.51*	1.4	9.39*	1.2	8.59*	1.3
Phosphorus (mg/dI)	5.2*	0.7	3.75	0.73	3.39*	0.8
AIP (U/L)	209.7*	37.6	211.5*	40.4	266.3*	59.7
OC (ng/ml)	3.86*	1.1	4.2*	1.2	8.6*	2.4
Dpd (nM/mM creat.)	6.5*	1.2	6.4*	0.92	8.6*	2.9
Hydroxyproline (mg/24h)	48.6*	13.5	26.2*	5.3	71.62*	20.1

* High significant difference
- Ap Spine B.D.: anteroposterior bone density.
- Lt femur B.D: Left Femur bone density.
- AIP: Alkaline phosphatase.
- Dpd: Deoxypyridinoline.
- OC.: Osteocalcin.

Regarding Calcium and phosphorous levels, the results of the present study revealed that there was no change in phosphorous level while there was decrease in calcium level in cases of osteopenia and osteoporosis. In addition the current data revealed a negative correlation between serum OC level and Ca level in osteoporotic women, although this correlation did not reach the level of significance.

Concerning urinary Dpd, the present study showed that the mean urinary Dpd level was significantly increased in osteopenic and osteoporotic women. There was positive correlation between OC and Dpd.

Discussion

Biochemical markers of bone turnover provide a means of evaluating skeletal dynamics that complements static measurements at bone mineral density (BMD) **(Looker et al., 2000).**

Bone mineral density (BMD) measured by densitometry is the elective parameter for the diagnosis of osteopenia and osteoporosis. American College of Preventive Medicine guidelines on osteoporosis screening **(Lim et al., 2009)** conclude that biochemical markers cannot replace BMD testing.

Increased bone turnover at menopause is driven by bone resorption after osteoclasts are recruited from bone marrow, which is caused by dropping of estrogen levels (**Kushida et al., 1995).** Therefore estrogen replacement therapy is indicated for postmenopausal women **(Hasley et al., 1998).**

Several studies indicated that screening for bone markers may be useful for improving the assessment of osteoporotic women in combination with bone mass

measurements. This could be helpful to detect the osteoporosis and ultimately of fractures and to monitor rapidly the efficacy of antiresorptive therapy **(Brown et al., 2008).**

Lee et al. (2000) reported that serum OC level was 10%higher in postmenopausal osteoporosis. The same results were obtained by **Dominguez et al., (1998).**

Several studies reported no significant difference of OC level between osteoporotic and normal women **(Yilmaz et al., 1999).**

The current data indicated the presence of an inverse correlation between OC and BMD. These results agree with Slovic **et al**, (1984). In addition, other study showed some degree of negative correlation between serum OC and BMD in osteoporotic women **(Yasumura** et **al, 1987).** These findings may indicate that higher rates of bone turnover can be associated with more rapid bone loss in osteoporotic women.

The same findings were also reported by **Ross** and **Knowlton (1998).** They found an increased relationship between bone mass and biochemical markers other than OC. On the other hand, they found no correlation between BMD and OC and they claimed that measurement of biochemical indices of bone remodeling does not predict the severity of bone loss after menopause.

The results of the present study revealed significant increase of serum AIP in the osteopenic and osteoporotic women comparing them with the normal women in each of the three studied groups.

These results are in agreement with those of **Dominguez et al., (1998).**

These findings suggested that total AIP still maintains a possible role as a first analysis to evaluate bone turnover in osteoporosis before requesting markers with greater specificity and sensitivity and more expensive.

The increased levels of the two indices of bone turnover namely AIP and OC suggest that mean bone turnover is higher in osteoporotic women and this does not support the concept that an absolute decrease in bone formation is the major cause of their bone loss **(Delmas et al., 1983).**

The results of the present study proved the presence of significant correlation between OC and AIP in cases of osteopenia and osteoporosis.

Brixen et al., (1989) found a significant correlation between OC and AIP in patients with high rate of bone turnover.

On the other hand **Kushida et al., (1995)** found no correlation between OC and AIP in cases of bone turnover.

They stated that the lack of correlation between OC and AIP may be explained as the AIP level is only a rough index of osteoblastic activity, since non-osseous tissues contribute to the serum pool of this enzyme.

Regarding Calcium and phosphorous levels, the results of the present study revealed that there was no change in phosphorous level while there was decrease in calcium level in cases of osteopenia and osteoporosis.

Yilmaz et al., (1999) stated, that the serum Calcium and phosphorous did not show any significant changes between normal and osteoporotic women.

In addition the current data revealed a negative correlation between serum OC level and Ca level in osteoporotic women, although this correlation did not reach the level of significance.

This observation suggests that the accelerated skeletal turnover rate, as indicated by the high OC level, is associated with a net loss of bone **(Yasumura et al., 1987).**

Yilmaz et al.(1999) & **Lee et al, (2000)** stated that, the bone resorption markers have higher diagnostic value for diagnosis of osteoporosis than the bone formation markers.

Concerning urinary Dpd, the present study showed that the mean urinary Dpd level was significantly increased in osteopenic and osteoporotic women. There was positive correlation between OC and Dpd.

Yilmaz et al., (1999) stated that the bone resorption marker, Dpd was significantly high in osteoporosis. Also,

they added that urinary Dpd level increase with severity of the disease. **Rosen et al., (1998),** reported that urinary Dpd level was significantly increased in osteoporosis, **Lee et al., (2000)** reported that urinary Dpd level was 50% higher in postmenopausal osteoporosis than in premenopausal women. Bone resorption markers are more efficient than bone formation markers **(Glover et al., 2008).**
Urinary Dpd level is valuable in discriminating osteoporosis possibly because of osteoclastic nature of the disease **(Rosen et al, 1998).**
The results of the present study revealed significant higher level of OHP in the third group (III) when compared to the other groups I&11.When comparing osteoporosis and osteopenic women in each of the three studied groups with normal women, there was higher level for OHP.
Eastell et al, (1993) stated that serum AIP and urinary OHP markers lack sensitivity and specificity and so can not be considered reliable indices to predict the complex abnormalities of bone remodeling in osteoporosis. Therefore, there have been great efforts to develop more sensitive biochemical markers of bone turnover **(Glover et al., 2009).**

The immunoassay of osteocalcin and assay of alkaline phosphatase are currently the most used markers for assessing bone formation. The best indices of bone resorption include hydroxyproline and dexoypyridinoline.

Conclusion:

As a result of this study it can be said that bone density measurements allow the diagnosis of osteoporosis before fractures occur, Biomarkers can identify patients with a high bone turnover, a situation that leads to rapid bone loss. These two diagnostic tools together can help identify osteoporosis in its earliest form so that preventative measures can be instituted.
It was found that the Egyptian women subjected to the present study are suffering from osteopenia from the age of 35 years old or may be earlier. Above the age of 55 (postmenopausal), it was found that 50% of women are osteopenic and osteoporotic.

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الدلالات البيوكيميائية لتغير العظام في السيدات المصريات في الأعمار المختلفة

ألفت عبد الظاهر خليل وخلود صلاح الدين رمضان
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إن هشاشة العظام مرض يصيب عظام الرجال والنساء حيث يكون مستوي التآكل في العظام أكبر من مستوي إعادة تكوينها. الهدف من هذا البحث هو الكشف عن بعض دلالات هشاشة العظام في دم وبول السيدات المصريات في مراحل عمرية مختلفة. شملت هذه الدراسة 100 سيدة قسمت إلي ثلاث مجموعات. المجموعة الأولي (33 سيدة) يتراوح أعمارهن بين 35-45 سنة, المجموعة الثانية (33 سيدة) تتراوح أعمارهن بين 45-55 سنة والمجموعة الثالثة (34 سيدة) أعمارهن أكثر من 55 سنة.

أجري قياس لكثافة العظام لكل السيدات وكذلك تم قياس الكالسيوم, الفسفور, الفوسفاتيز القلوي وأوسيتوكالسين في دم السيدات وكذلك تم قياس كل من هيدروكسي برولين, ديأوكسي بيريدينولين وكرياتينين في البول.

أسفرت النتائج عن وجود زيادة في كل من الفوسفاتيز القلوي وأوسيتوكالسين في دم السيدات المصابات بهشاشة العظام ووهن العظام وكذلك زيادة في بيريدينولين هيدروكسي برولين في البول. بينما كان هناك نقص في كالسيوم الدم في هؤلاء السيدات.

نستنتج من هذه الدراسة أن نسبة كبيرة من السيدات المصريات يعانين من وهن العظام من سن 35 سنة أو ربما أقل. وبالنسبة للسيدات فوق سن 55 سنة وجد أن 50% منهن يعانين من وهن وهشاشة العظام.