ORIGINAL ARTICLE

FACTORS CAUSING EARLY OSTEOPOROSIS IN PERIMENOPAUSAL WOMEN

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Background: Osteoporosis is a major problem particularly in women. The objective of this study was to evaluate effects of urbanization, high socio-economic status, and decreased ambulation for early osteoporosis in perimenopausal women. **Methods:** This was a descriptive cross-sectional study carried out in Postgraduate Medical Institute, Hayatabad Medical Complex, Peshawar from June to Aug 2012. Our study population was peri-menopausal women assessed radiographically for osteoporosis. The levels of carboxy-terminal collagen cross-links (CTX-I) as a marker of bone degradation were determined. These women were randomly selected and screened for osteoporosis. In addition, haemoglobin, erythrocyte sedimentation rate (ESR), serum calcium and serum alkaline phosphatase levels were determined. Radiographic grading of osteoporosis was done according to Singh index as I to VI. **Results:** High levels of CTX-I were observed in perimenopausal women who were radiographically diagnosed as osteoporotic patients. High socio-economic class also is predisposed to osteoporosis. Decreased ambulation was significantly associated with increased levels of CTX-I. **Conclusion:** Both decreased ambulation and high socioeconomic class had significant association with increased levels of serum CTX-I.

Keywords: Osteoporosis, CTX-I, Perimenopausal women

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INTRODUCTION

CTX is a marker of bone degradation. It is derived from the enzymatic degradation (hydrolysis) of type I collagen; CTX is a peptide related to regions of cross linking with pyridinoline.[1,2] Type I collagen comprises over 90% of the total bone protein. High levels of CTX-I are indicative of excessive bone resorption and indicate osteoporosis. It is a sensitive marker for bone resorption in osteolytic diseases such as osteoporosis and osteoarthritis.[1] Bones continuously remodel according to body requirement and resources. Osteoclasts are responsible for enzymatic hydrolysis of type I collagen, a helical protein which is 90% of bone proteins. Acidic and neutral proteases breakdown collagen into fragments, releasing cross-linked N-terminal and C-terminal telopeptide (CTX-I).[2] CTX-I, as biochemical marker of bone degradation, is the most sensitive marker to assess bone degradation and formation.[3] Christian Fledelius[4] in 1997 described CTX as product of bone degradation.

Osteoporosis is a condition in which bone mass is decreased without any change in chemical composition of the bone. When bone is not able to withstand normal daily stresses due to osteoporosis, it is considered as pathology of bone. There is high risk fracture when an ordinary skeletal stress is applied. In women the major cause of osteoporosis is menopause. Majority of post-menopausal women suffer from osteoporosis. A person with osteoporosis is also emotionally upset. In osteoporosis, commonly fractured bones are lumbar vertebrae, distal radius and femoral neck. According to localization and aetiology in the skeleton, osteoporosis is mainly divided into generalized and localized classes. These are further divided into primary and secondary osteoporosis.

Primary osteoporosis is labelled so when there is no cause, while secondary osteoporosis results from any disease, deficiency or any medication. Types of primary osteoporosis are juvenile osteoporosis and idiopathic osteoporosis. The idiopathic is further classified into post-menopausal osteoporosis (type I) and senile or age-related osteoporosis (type II). Causes for secondary osteoporosis are congenital, hypogonadism, endocrine disorders, haematological or neoplastic disorders, inflammatory diseases and medications.

History taking is an important step in identifying the cause of osteoporosis. Risk factors play a very important role in the initiation of the disease. Risk factors for osteoporosis are reduced bone mineral density and advanced age. Both have strong relationship with the incidence of bone fractures and disability. There are many other risk factors which have been identified and are considered to play a major role in osteoporosis. These are female sex, early menopause, perimenopausal age, early menarche, androgen and oestrogen deficiency and genetic factors (family history of osteoporosis).

Osteoporosis is a major problem particularly in women. In Pakistan, it most commonly affects women of 45 years and above. They frequently visit orthopaedic

clinics with complaints of body aches, particularly backache.

PATIENTS AND METHODS

This descriptive, cross-sectional study was carried out in Postgraduate Medical Institute (PGMI), Hayatabad Medical Complex, Peshawar, Pakistan to determine levels of CTX-I as a marker of bone degradation in radiographically assessed peri-menopausal women. These women were randomly selected and screened for osteoporosis. Informed consent was obtained from each subject. Ethical approval for the study was obtained from the Institutional Ethical Research Committee (IERC) of PGMI, Peshawar.

Sample size was 100 subjects, using 30% proportion of osteoporosis, 95% confidence level and 5% margin of error according to WHO standard for sample size determination. The age of the women ranged between 45 and 55 years. Variables like age, age at marriage, education, husband's education, occupation and monthly income along with number of pregnancies, number of still births and number of live children were recorded. ESR, serum albumin, serum calcium, serum alkaline phosphatase were determined and those having normal values of these variables were excluded from the study. The subjects having an ESR above 25 mm in 1st hour, alkaline phosphatase above 260 IU/L, serum albumin above 3 gm/dl and subjects with comorbid diseases and any history of joint diseases were also excluded from the study.

The analytic work was done in Pakistan Medical Research Council Research Centre, Khyber Medical College, Pathology Laboratory of Institute of Kidney Diseases and PGMI, HMC, Peshawar. Subjects were also assessed for their lifestyle, education, husband's education, occupation, monthly income, previous family history regarding the disease, previous medications like steroids, number of pregnancies, age in years, ambulatory status as community ambulant, household ambulant, and/or being bed ridden.

Haemoglobin in gm/dl, ESR by Westergren method as mm after 1st hour, serum albumin (g/dl), serum Ca as mg/dl, serum alkaline phosphatase as IU/litre, radiographic grade of osteoporosis according to Singh index as I–VI and CTX-I level in pg/ml were estimated. Association of parameters and their significance were sorted out on SPSS-17. All individual variables were analysed as independent variables. Chi-square test was applied to determine the association of increased levels of CTX-I with various variables and hence with osteoporosis.

RESULTS

Eighty percent of the study population was from urban areas and had an income of above PK Rs. 20,000 per month. Urbanization had a significant association with increased levels of CTX-I (p=0.05). High socioeconomic status showed a significant association with increased levels of CTX-I and osteoporosis (p=0.000). Ambulatory status also showed significant association (p=0.000) with increased levels of CTX-I. Education, husband's education and occupation had no association with increased CTX-I level or osteoporosis.

The major bulk (74%) of the study population was from urban areas while 9% came from rural areas and the remaining 17% belonged to tribal areas. All cases of increased CTX-I were found in urban population (p=0.05) (Table-1).

Three out of four household ambulant women had an elevated (5 times normal value) CTX-I levels and one had normal level of CTX-I (Table-2).

Eight percent of study population had a monthly income of PK Rs. 5,000–10,000, 13% had income range between PK Rs. 10,000–2 0,000 while 79% of the subjects were having income above PK Rs. 20,000 from all sources. When cross-tabulated with levels of CTX-I, monthly income showed a significant association (p=0.006) using Chi-square test (Table-3).

Table-1: Cross-tabulation between demographic distribution and serum CTX-I

Serum CTX-I (pg/ml)	Rural	Urban	Tribal	Total
50–410	7	30	11	48
411–920	0	19	2	21
921–1230	1	21	2	24
1231–1640	1	1	2	4
1641–2050	0	3	0	3
Total	9	74	17	100

p=0.05

Table-2: Cross-tabulation between serum CTX-I and ambulatory status of study group

Serum CTX-I (pg/ml)	Community	Household	Total
50-410	47	1	48
411-920	21	0	21
921-1230	24	0	24
1231-1640	4	0	4
1641-2050	0	3	3
Total	96	4	100

p=0.000

Table-3: Cross-tabulation between monthly income and levels of Serum CTX-I of study group

Serum CTX-I (pg/ml)	Monthly Income (×1,000 Rupees)			Total
	5–10	10–20	>20	
50–410	1	2	45	48
411–920	5	5	11	21
921–1230	2	6	16	24
1231–1640	0	0	4	4
1641–2050	0	0	3	3
Total	8	13	79	100

p=0.006

DISCUSSION

None of the socio-demographic variables like age, age at marriage, number of pregnancies, number of live births, number of still births, number of alive children, had any association with osteoporosis or increased CTX-I levels. All the individual variables were analysed as independent variables. None had any positive or negative association. Majority of the study population was from urban areas and had a monthly income of above 20,000 rupees. Those with increased levels of CTX-I were from urban population having income above 20,000 rupees per month. This shows a statistically significant association with increased CTX-I and osteoporosis. Education, husband's education and occupation had no association with increased CTX-I or osteoporosis.

Increasing age is a known risk factor for osteoporosis because it is associated with increased bone degradation.[5,6] In this study, 16% of the subjects were housewives while the rest were on government jobs. Majority of the study population was below 50 years of age. The age in itself did not appear to be associated with osteoporosis (Singh index) or increased CTX-I. This has resulted because comparatively older women suffering from osteoarthritis and other chronic diseases were not included in the study.

Van Hemert *et al*[5] reported that number of children and period of lactation are significant factors for osteoporosis, the same could not be observed in this study as the descriptive analysis for individual values did not reveal any association between number of pregnancies or their outcome or number of children with osteoporosis.

Serum CTX-I was estimated in laboratory and Singh index was recorded from digital anterio-posterior radiograph of pelvis. Very few subjects in grade IV and grade V had normal CTX-I levels. On the other hand, increased CTX-I was noted in women with grade VI, which explains bone degradation without the radiological evidence. This shows the quality of the CTX-I as an early indicator of bone degradation. This is also supported by Greenspan *et al*[7] who described CTX-I as more reliable marker for bone antiresroptive therapy and found that serum CTX-I levels are more sensitive markers of response to treatment.

Population based cohort study on 1,044 elderly women from Malmo OPRA study described CTX as indicator for bone degradation. The project lasted for nine years and revealed a significant association of CTX and osteoporosis. OFELY cohort study followed 435 post-menopausal women for five years, and concluded that CTX has an association with decreased mobility of their subjects and osteoporosis. EPIDOS cohort enrolled 800 women above 75 years, followed them for three years and found serum CTX and hip bone BMD as effective tool for monitoring osteoporosis.

Cross-tabulation of serum CTX-I against the grades of Singh index in this study showed three subjects with grade IV osteoporosis. One of these had a value of CTX-I three times normal while two had 5 times the normal value. Out of 18 subjects falling in grade V, two subjects had normal value, one had 2 times, six had 3 times, four had 4 times and one subject had 5 times the normal value. Higher level of CTX-I indicates increased bone breakdown, which is significantly associated not only with decreased grades of Singh index, but also related to limited mobility.

CONCLUSION

Estimation of CTX-I as a marker of bone collagen degradation is a reliable and cost-effective biochemical tool. In women aged 45–55 years, bone degradation is significantly associated with urbanization, high socioeconomic class and ambulation. There is significant correlation between radiographic evidence of osteoporosis and biochemical marker.

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