CTX1 is A Better Index to Evaluate The Severity of Osteoporosis then Radiographic Index

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ABSTRACT

Objective: To illustrate that CTX1 is the far better tool to evaluate the severity of osteoporosis then radiographic index (Singh index) in perimenopausal women.

Material and Methods: This descriptive cross sectional study was done on 100 subjects, in the tertiary referral health care facilities of Peshawar via PGMI Hayatabad Medical Complex, Peshawar, Pakistan. The study was done in six months' time period. Levels of CTX1 as a marker of bone degradation in radiographically assessed perimenopausal women were determined. These females were randomly selected and screened for osteoporosis. Radiographic grade of osteoporosis according to Singh index as 1-6 and CTX 1 level in pg/ml was taken.

Results: High levels of CTX1 were observed in perimenopausal osteoporotic women, which were radiographically normal.

Conclusion: The results of this study propose that CTX1 levels are the more reliable tool for assessing osteoporosis as compared to radiographic index.

Key Words: Osteoporosis, CTX1, Perimenopausal Women, Singh Index.

INTRODUCTION

Osteoporosis is a worldwide problem of old age due to increased resorption not matched by bone formation causing fractures which leads to disability and high costs to society[1,2]. Osteoporosis is a condition in which bone mass is decreased without having any change in chemical composition of the bone. Osteoporosis is then considered as pathology of bone, when its strength is not able to withstand normal daily stresses[3]. There is a high risk of fractures when an ordinary skeletal stress is applied. Majority of post-menopausal women suffer from osteoporosis[4].Worldwide over 200 million people are suffering from osteoporosis and of these 30% are postmenopausal women residing in Europe and United State of America .A study in Pakistan revealed that the prevalence of osteoporosis is more in Pakistani women in their child bearing age group[5].Bone loss in women starts slowly and speeds up by the time of menopause, at the age of or after the age of 50 years .Moreover the frequency of post-menopausal osteoporosis is the highest in women at the age of 50 – 70 years. In Pakistan it most commonly affects women of above 45year of age.

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Work up for Osteoporosis includes: Complete blood count (CBC), serum calcium levels, serum alkaline phosphatase, serum albumin, X –ray, Bone Mineral Density (BMD), Urinary NTX (N-terminal telopeptide) and serum CTX (C-terminal telopeptide). 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. 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[6].

CTX1, as biochemical marker of bone degradation, is the most sensitive marker to assess bone degradation and formation[7].American Society for Bone and Mineral Research investigated the use of bone markers for monitoring of intervention for bone loss in early menopausal women and to assess the relationships between these markers and changes in BMD. This study concluded that serum CTX1 as bone resorption marker is a better indicator than bone formation marker[8].

Singh index is a simple and inexpensive tool for evaluating quality of bone in patients with bony diseases such as osteoporosis, osteoarthritis and rheumatoid arthritis. Estimation of Singh index is made on digital pelvis radiograph anterio-posterior view. There are six grades of Singh index which help in

evaluation of severity and extent of bone disease and involvement[9].(Table 1 and Figure 1).

The rationale behind this study is to generate local statistics as limited local data is available on this aspect. The results of this study will be shared with other orthopedic surgeons and rheumatologists to make them aware about the local magnitude of the problem and on the basis of results of this study if theCTX1 is the better tool to evaluate the severity of osteoporosis then radiographic index (Singh index) in perimenopausal women then we will be able to recommend not only early screening of all patients but also early referral to tertiary care.

Table 1: Grades of Singh index

Grade	Description
VI	All normal trabecular groups are visible and upper end of femur seems to be completely occupied by cancellous bone.
V	Principal tensile and principal compressive trabeculae are accentuated and Ward's triangle appears prominent.
IV	Principal tensile trabeculae are markedly reduced but can still be traced from lateral cortex to upper part of the femoral neck.
III	There is a break in the continuity of the principal tensile trabeculae opposite the greater trochanter and this grade indicates definite osteoporosis.
II	Only principal compressive trabeculae stand out prominently and remaining trabeculae have been essentially absorbed.
I	Principal compressive trabeculae are markedly reduced in number and are no longer prominent.

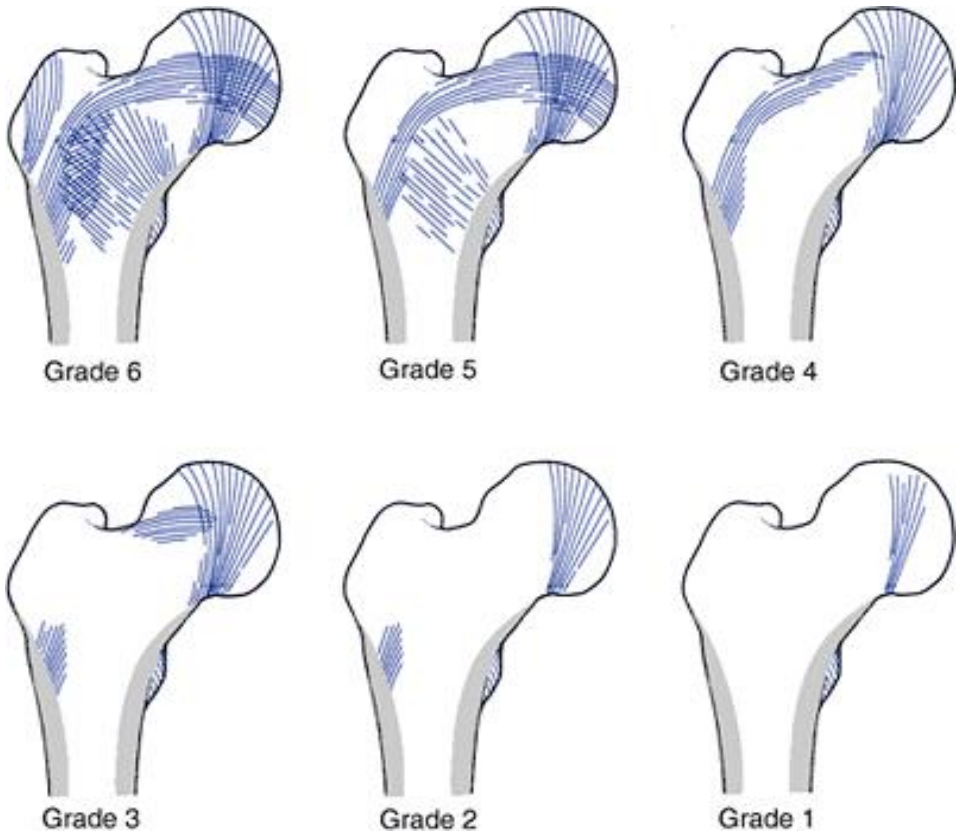

Fig 1: Singh Index

Singh's index grades osteopenia from normal (grade 6; all trabecular groups are visible) to definite (grade 3; thinned trabeculae with a break in the principal tensile group) to severe (grade 1; only the primary compressive trabeculae are visible, and they are reduced) based on the ordered reduction in trochanteric, tensile, and ultimately primary compressive trabeculae. The grade is determined from a true antroposterior projection of an intact proximal femur. (Adapted from Singh M, Nagrath AR, Maini PS. Changes in trabecular pattern of the upper end of the femur as an index of osteoporosis.[9].

MATERIAL AND METHODS

The descriptive cross sectional study was carried out in the tertiary referral health care facilities of Peshawar via PGMI Hayatabad Medical Complex, Peshawar, Pakistan to determine levels of CTX1 as a marker of bone degradation in radiographically assessed perimenupausal women. The analytic work was done in PMRC Research Centre, Khyber Medical College, Peshawar and pathology labs of Institute of Kidney Diseases and Post Graduate Medical Institute, Hayatabad Medical Complex, Peshawar. Study population was women between the age group of 45-55 years of age in their perimenopausal period having no complaints of joint or bone pains were included, while women with history of osteoarthritis, rheumatoid arthritis and any other bony disease were excluded.

Sample size was 100 subjects, using 30% proportion of osteoporosis, 95% confidence level and 9% margin of error under WHO (World Health Organization) software for sample size determination. This study was under taken on 100 perimenopausal women in Hayatabad Medical Complex hospital. These females were randomly selected and screened for osteoporosis. After explaining aims and objectives, informed consent was taken from each subject for participation in study. Ethical approval for the study was taken from the Institutional Ethical Research board (IERD) at Post Graduate Medical Institute, Hayatabad Medical Complex Peshawar.

The research data was subjected to statistical analysis, using Chi-square test on SPSS version 17. The numerical and categorical data was presented as mean to evaluate the levels of CTX1 in perimenupausal women with their radiographic grades and also with serum calcium, albumin, alkaline phosphatase, ESR and hemoglobin levels. Significant levels among the mean of different variables were expressed in terms of 'P' value, 95% confidence interval (Cl), P< 0.05 was considered as significance.

RESULTS

There were total 100 females in the study with age range of 45-55 years, belonging to both rural and urban population.

Serum CTX1 was plotted against Singh index. Only three subjects were found in grade IV, one of these subjects had levels of CTX1 three times of control and two subjects had five times of control value. Fourteen subjects were found in grade V, 2 of them had normal value of CTX1, one had double the normal value, six had triple, four had 4 times and one subject had five times the normal value of CTX1.

Table 2 shows the mean values of CTX1 for grades VI, V and IV, which are 454.9639, 1047.6429 and 1672.000 respectively. ANOVA was applied giving a P value of 0.05 showing a significant correlation with Singh index i.e. serum levels of CTX1 and radiographic index are negatively correlated with one another.

Higher values of CTX1 and lower grade of Singh index were recorded in the study population. Singh index of grade IV was observed to have 4 to 5 times of the control value. Higher levels of CTX1 indicate increased bone breakdown, which is not only significantly associated with decreased grades of Singh index, but also significantly correlated with below normal hemoglobin and household ambulation or limited mobility.

Table 2: Means for grades of Singh index among the study group.

Singh Index	Mean	N	Std. Deviation
Grade IV	1672.0000	3	590.63694
Grade V	1047.6429	14	464.55050
Grade VI	454.9639	83	264.61175
Total	574.4500	100	416.55612

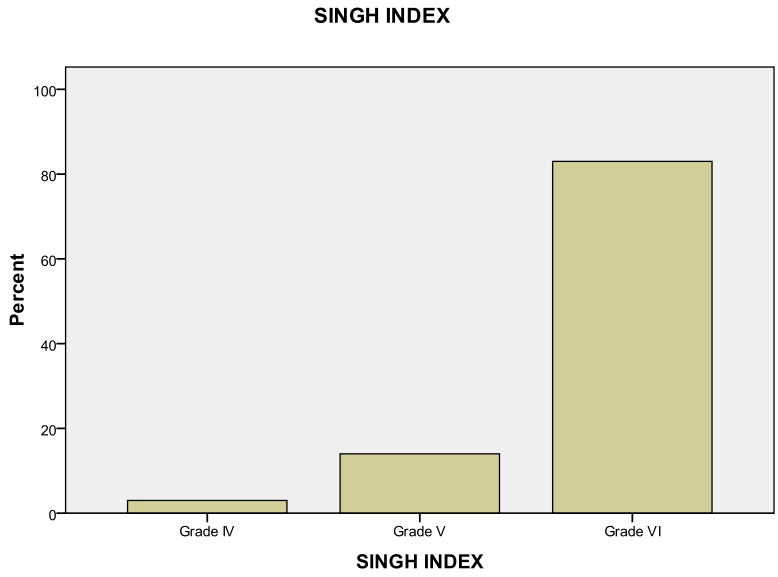

Figure 2: Grade of Singh Index in the study population

Table 3: Cross tabulation between the levels of serum CTX1 and grades of Singh index of the study group

Serum CTX 1 (pg/mL)	SINGH INDEX			Total
	Grade IV	Grade V	Grade VI	
50-410	0	2	46	48
411-920	0	1	20	21
921-1230	1	6	17	24
1231-1640	0	4	0	4
1641-2050	2	1	0	3
Total	3	14	83	100
P value=0 .000				

Table 4: Cross tabulation between the levels of serum CTX1 and grades V1 & 1-V of study group

Serum CTX1(pg/mL)	SINGH INDEX		Total
	Grade VI	Grade I-V	
50-410	46	2	48
411-3000	37	15	52
Total	83	17	100
P Value =0.001			

DISCUSSION

Ljunggren'in 1992 and later Christian Fledelius 1997described CTX1 as product of bone degradation[10].The increased prevalence of osteoporosis with increasing age particularly in women provided a basis for this study. It was conducted on 100 females having an age range of 45 – 55 years.

Majority of the study population in this study were below 50 years of age. In the age group of the present study, the age in itself did not appear to be associated with osteoporosis (Singh index) or increased CTX1. It

was so because comparatively older women suffering from osteoarthritis and other chronic diseases were excluded.

Serum CTX1 was estimated in laboratory and Singh index was recorded from digital anterio-posterior radiograph of pelvis. CTX1 value was entered. Very few subjects in grade IV and grade V had normal CTX1 levels. On the other hand increased CTX1 was noted in grade VI women, which explains bone degradation without the radiological evidence. This shows the quality of the CTX1 as an early indicator of bone degradation. This is also supported byRosen H. N.[11]who described CTX1 as more reliable marker of bone antiresoptive therapy, and found that serum CTX1 levels are more sensitive marker of response to treatment.

PramuditolJ.T[12] in 2007described osteoporosis as brake in continuity of primary tensile trabacule of femur. The inability of structural integrity to withstand normal stress results in non traumatic fracture. He described dexa scan and BMD (bone mineral density) to be the gold standard for osteoporosis but his study was based on radiographic appearance of proximal femora and Singh index. The author elaborated the accentuation of principle tensile and principle compressive trabacule in stage V along with prominence of ward triangle. Population based cohort study on 1044 elderly women from Malmo oprastudy[13]described CTX1 as indicator for bone degradation. The project lasted for nine years and revealed a significant association of CTX and osteoporosis. OFELY cohort study[14]followed 435 post-menopausal women from for five years, and concluded that CTX has an association with decreased mobility of their subjects and osteoporosis.

EPIDOS cohort[15]enrolled 800 females above 75 years, followed them for three years and found serum CTX1 and hip BMD as effective toll for monitoring of osteoporosis.Cross tabulation of Serum CTX1 against the grades of Singh index in this study showed three subjects with grade 1V osteoporosis. One of the subjects had a value of CTX1 three times of normal value while two had 5 times of that of normal value. Out of eighteen subjects falling in grade V, two subjects had normal value that of control, one had double, six had triple, four had 4 times and one subject had 5 times the value of control.A prospective trial of 960 elderly females in nursing home failed to show statistical significance of CTX1 for fracture risk estimation in Australia.

Means for grade IV from 3% of study population was 1672 ± 590.63, whereas means for grade V from 14 subjects was 1047.6429 ± 464.550.83% study population had mean for grade VI as 454.9639 ± 264.611 and the P value when calculated for all the means of these given grades by ANOVA was 0.000 i.e. $P < 0.05$.

Malmo trial[16]was conducted on random population enrolling 1040 women above 75 years of age. Follow up of 3-6 years failed to show significant association of CTX1 and fracture estimation. Increased CTX1 and radiographic index of osteoporosis seemed to be significantly associated because higher values of CTX1 were observed in subjects of lower grade of Singh index. Singh index of grade 1V was observed to have 4 to 5 times of the control value. Higher level of CTX1 indicates increased bone breakdown, which is significantly associated not only with decreased grades of Singh index, but also related to below normal hemoglobin and household ambulation or limited mobility.

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