ORIGINAL ARTICLE

# COMPARATIVE STUDY OF SERUM CALCIUM LEVEL BETWEEN POSTMENOPAUSAL AND PREMENOPAUSAL WOMEN

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## ABSTRACT

In postmenopausal women, more significant bony consequences are associated with low blood calcium levels. A observational cross-sectional study was conducted in the Department of Biochemistry, Dhaka Medical College, Dhaka from July 2014 to June 2015. Serum calcium levels were compared between postmenopausal women as cases and premenopausal women as controls. The study sample size was 100 of which 50 were postmenopausal, and 50 were premenopausal. Mean (±SD) of serum calcium level was significantly higher in the premenopausal group than in the postmenopausal group. Serum calcium level was 8.66±0.43 mg/dL in postmenopausal women and 9.12±0.59mg/dL in premenopausal women. Both the values were within the normal reference range, but the difference was statistically significant with a p-value of 0.001. By this research work, it is observed that postmenopausal women are more prone to develop osteoporosis with a decreased serum calcium concentration. Routine check-up of this biochemical parameter may provide valuable information for preventing osteoporotic fractures in postmenopausal women.

**Key words:** Postmenopausal, Menopausal, Calcium

## Introduction

Bone is a dynamic tissue that is continuously resorbed, replenished, and rebuilt. Several different kinds of bone cells perform these functions. Osteoblasts synthesize, transport, organize many matrix proteins, and start the mineralization process. Osteoblasts change into osteocytes when they are encircled by newly deposited organic matrix. Osteocytes aid in regulating the micro-environment's calcium and phosphate concentrations. By creating an acidic environment with the help of a proton-pump system and breaking down the organic component with the release of proteases, osteoclasts remove the mineral[1]. Therefore, osteoclasts and osteoblasts are the principal cell types engaged in bone resorption and deposition. The former is linked to bone resorption whereas the latter is linked to bone deposition[2].

A solid mineral phase closely associated with an organic matrix, of which 90–95 percent is type I collagen, makes up the extracellular component of bone. Some of the proteins help to arrange collagen fibrils while others affect mineralization and the matrix's ability to bind the mineral phase[3].

The skeleton's structural foundation is the calcium ion. Growing research supports the role of nutrition in maintaining the health of bones and joints[4]. The skeleton contains 99% of the

body's calcium, predominantly as extracellular crystals of unknown structure with a composition approaching that of hydroxyapatite[5]. Due to the demand of a rapidly developing skeleton, calcium needs are considerable during adolescence. Until menopause, when the rate of bone resorption rises in correlation with the reduction in ovarian estrogen production, the demand for calcium stays constant[6].

Menopause which affects women between the age of 45 and 55, is marked by a number of psychological and biological changes[4]. The monthly sexual cycle becomes irregular, ovulation fails to occur during many of the cycles and ultimately there is cessation of the cycles[7]. In basic terms, women's postmenopausal stage is an estrogen deficient state[8]. Estrogens have a significant impact on bone remodeling in women by preventing the generation of interleukin IL-6, which lowers bone resorption and regulates the timing of osteoclast apoptopsis. Osteoclasts live longer when there is a lack of estrogen[4]. Additionally, estrogen insufficiency may cause calcium loss via having an indirect impact on the extraskeletal calcium homeostasis. Postmenopausal women have decreased intestinal calcium absorption[7].

Estrogen has a positive impact on bone mass and calcium balance. They lessen bone loss, while estrogen promotes linear bone development and causes epiphyseal closure in adolescent girls. Loss of bone mineral content, an increase in stress fractures, and postmenopausal osteoporosis are all linked to long-term estrogen deficiency[5]. This mechanism is driven by linked osteoblastic and osteoclastic-activity, which contrasts with the relatively high daily rates of closely matched calcium fluxes into and out of bone. These delay changes in total skeletal calcium concentration[3].

After menopause, bone turnover accelerates very quickly. The main cause of this problem is an inadequate supply of estrogen. Cytokines released by bone marrow cells and blood monocytes have a role in how estrogen affects bone mass. These cytokines promote osteoclast activity and recruitment by upregulating receptor activator of nuclear factor kappa-B (RANKL) and downregulating osteoprotegerin (OPG) expression. When compensatory osteoblastic activity does not keep up with bone resorption, the condition is referred to as a high turnover variant of osteoporosis[1].

The differentiation and function of osteoclasts are modulated by a number of growth factors and cytokines, including interleukin-1, interleukin-6, interleukin-11, tumor necrosis factor, and interferon. Most hormones that affect osteoclast activity affect osteoblasts' ability to communicate via RANK ligand and macrophage colony-stimulating factor rather than directly targeting osteoclasts[3].

For the diagnosis and follow-up of metabolic bone disease, biochemical markers of bone turnover have been proven to be useful[9]. These indicators reveal changes in bone remodeling far sooner than radiography changes would suggest. Furthermore, these indicators now make it feasible to assess the effectiveness of anti-resorptive medications. They offer untapped potential in assessing patients who are at risk of experiencing postmenopausal women's rapid bone loss[10].

## Materials and Methods

This observational cross-sectional study was conducted in the Department of Biochemistry at Dhaka Medical College from July 2014 to June 2015. Informed consent was obtained from individual participants after a detailed explanation of the nature, purpose, and procedure used. Ethical approval was obtained from the Ethical Review Committee of the Dhaka Medical College. Purposive and convenient sampling

techniques were used, strictly maintaining inclusion and exclusion criteria. A total of 100 women were selected as the study population. Postmenopausal women of 45 to 65 years were selected from apparently healthy adult individuals attending the outpatient department of Dhaka Medical College as cases (Group A), and 50 premenopausal women were chosen as controls (Group B) with an age range of 35 to 45 years. Initial evaluation was done by taking proper history and clinical examination, and blood pressure, height, and weight were recorded in a preformed data sheet. The subjects with known hormonal abnormality, acute and chronic liver disease, any debilitating illness such as chronic renal diseases, malignancy, arthritis, bone diseases, or taking calcium, vitamin D, bisphosphonate, hormone therapy, or drug for convulsive disorder were excluded. The subjects with pregnancy, lactating mother, thyroid and parathyroid abnormalities, acute and chronic renal failure, acute and chronic liver disease, bone disease, malignancy, history of hysterectomy, or calcium therapy were not included-in control group. With all aseptic precautions, blood samples were collected from each study subjects. Statistical analysis was performed using the SPSS version 21.0 for Windows, and statistical significance was set at $p < 0.05$.

## Results

The present case-control study was designed to compare serum calcium levels-between postmenopausal and premenopausal women. For this purpose, 100 adult women were enrolled as study participants. Among them 50 women were premenopausal represented as controls and 50 postmenopausal women were taken as cases. Along with baseline information, blood sample was collected and analyzed for serum calcium in both cases and controls. All data were processed to compute mean and standard deviation.

Differences of means among two groups were compared with unpaired ttest, more than two groups were compared by ANOVA and determination of correlation between variables was done by Pearson's correlation test. For all statistical analyses $p < 0.05$ were considered as significant. Following results and observations were obtained in the present study.

Table I shows physical findings of the study subjects. Pulse, systolic BP and diastolic BP were significantly higher in postmenopausal group than that of premenopausal group. Mean BMI was almost same in both groups. There are 7 postmenopausal overweight women in group A and 3 premenopausal overweight women in group B.

**Table I:** Physical status of study subjects

| Physical findings | Group A (n=50) Postmenopausal Mean ± SD | Group B (n=50) Premenopausal Mean± SD | p value |
|---|---|---|---|
| Pulse | 76.0±5.0 | 73.0±6.0 | 0.011* |
| Systolic BP (mmHg) | 128.0±11.0 | 113.0±10.0 | 0.001* |
| Diastolic BP (mmHg) | 81.0±7.0 | 71.0±7.0 | 0.001* |
| BMI ($kg/m^2$) | 23.2±2.1 | 22.9±1.4 | 0.422 |

*Independent t-test was done to measure the level of significance. *Statistically significant; p-value <0.05 is considered as significant.*

Table II shows biochemical findings of the study populations. Serum calcium was significantly higher in group B than that of group A.Table III shows serum calcium was elevated as per the increment of YSM the (year since menopause) and the pvalues were 0.001.

**Table II:** Comparison of serum calcium levels between study groups

| **Parameter** | **Group A (n=50) Postmenopausal Mean ± SD** | **Group B (n=50) Premenopausal Mean± SD** | **p value** |
|---|---|---|---|
| Serum calcium (mg/dL) | 8.66±0.43 | 9.12±0.59 | 0.001* |

*Independent t-test was done to measure the level of significance; *Statistically significant; p-value <0.05 is considered as significant*

**Table III:** Levels of serum calcium of cases according to the year since menopause.

| Investigations | Group A | | | | p value |
|---|---|---|---|---|---|
| | 1−5 YSM Mean ± SD (n=10) | 6−10 YSM Mean ± SD (n=15) | 11−15 YSM Mean ± SD (n=15) | >15 YSM Mean ± SD (n=10) | |
| S. Calcium (mg/dL) | 8.46±0.39 | 8.67±0.43 | 8.73±0.43 | 8.78±0.46 | 0.001* |

*ANOVA test was done to measure the level of significance; *Statistically significant;p value <0.05 is considered as significant.*

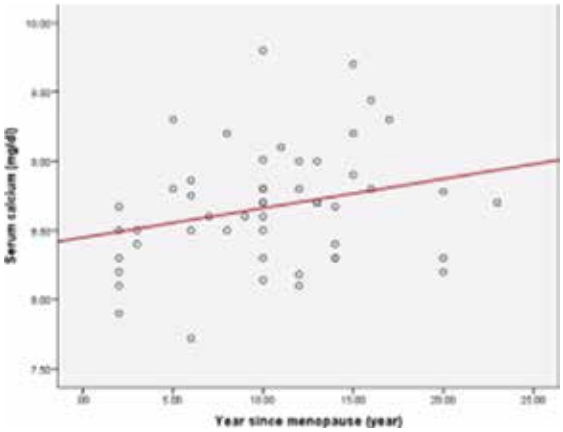


**Fig 1:** Correlation of the year since menopause (YSM) with serum calcium in postmenopausal subjects. Pearson's correlation, r is 0.261 with a p-value of 0.067. Serum calcium was positively but not significantly correlated with YSM in all study subjects.

## Discussion

The present case-control study was designed to observe changes in biochemical parameter of bone turnover namely serum calcium in 50 cases (postmenopausal women) and 50 controls (healthy premenopausal women) and it was compared between groups.

The age of the study participants ranged from 35 to 65 years in this present study. The mean age ±SD of cases and controls was 59.6±5.8 and 39.8±2.0 years respectively. As the baseline investigation the blood pressure of the cases and controls were measured, mean SBP±SD in cases and controls were 128±11.0 and 113.0±10.0 mm of Hg respectively and the mean DBP±SD in case and control were 81.0±7.0 and 71.0±7.0 mm of Hg respectively. Both the SBP and DBP has significant difference ($p<0.001$) between cases and controls, but they were normotensive for age. Both the groups were selected from apparently healthy people. Mean BMI was exactly same in both groups.

The result of the present study showed that the serum calcium concentration was significantly reduced in postmenopausal women with 8.66±0.43 mg/dL, compared to premenopausal women 9.12±0.59 mg/dL with a significant **p-**value of 0.001. These results were in line with a number of researches conducted by other authors[4,7,8-14].

Estrogen exerts a major effect in women on bone remodeling by inhibiting interleukin-6 production that reduces bone resorption and also controls the timing of osteoclast apoptosis. Therefore, osteoclasts live longer as a result of estrogen insufficiency. Intestinal calcium absorption decreases in postmenopausal women. Both these two pathophysiological phenomena are involved in decreased level of calcium in postmenopausal women[4].

In present study we obtained serum calcium concentration 8.46±0.39 mg/dL, 8.67±0.43 mg/dL, 8.73±0.43 mg/dL and 8.78±0.43 mg/dL for 1−5 YSM, 6−10 YSM, 11−15 YSM and >15 YSM respectively. A gradual increment of serum calcium level was observed after menopause with increase in years. Serum calcium level was decreased during early postmenopausal women compared to late postmenopausal women. There was increased loss of bone density for 5−6 years immediately following menopause due to sudden drop in estrogen levels and then reaching a plateau phase in which the bone loss attains almost a constant rate with a little variation. These

observations are consistent with the results of the study conducted by Indumati et al and Sachdeva et al[9,10]. A study conducted by Indumati et al-showed significant difference of calcium concentration between early and late postmenopausal women[9].

## References


1. Rosenberg AE, Bones, Joints and Soft tissue tumors. Kumar V, Abbas AK, Fausto N, Aster JC. Robbins and Cotran Pathological Basis of Disease. 8th ed., Philadelphia: Saunders Elsevier,1205–1255.
2. Murray RK and Keeley FW. Extracellular Matrix. 28th rev ed. NewYork: McGraw –Hill, 2009. Murray RK, Bender DA, Botham KM, Kennelly PJ, Rodwell VW, and Weil PA, Harper's Illustrated Biochemistry 2009:527–544.
3. Brighurst FR, Demay MB, Krane SM, Kronenberg HM. Harrison's principles of internal medicine. 18th rev ed., United States of America: Mc Grow Hill, 2012.
4. Bhale DV, Ansari HA. Study of serum calcium levels in postmenopausal women of Aurangabad District. International Journal of recent trends in science and technology 2014; 9(3): 332–333.
5. Endres DB and Rude RK. Disorder of Bone. 6th ed., Philadelphia: Saunders Elsevier, 2008. Burtis CA, Ashwood ER, Burns DE. Tietz Fundamentals of Clinical Chemistry; 711–734.
6. Heaney RP, Bilezikian JP, Holick MF, Nieves JW, Weaver CM. The role of calcium in peri- and postmenopausal women: 2006. The Journal of the North American Menopause Society 2006; 13(6): 862–877.
7. Qureshi HJ, Ghulam H, Jafary ZA, Bashir MU, Latif N, Riaz Z. Calcium status in premenopausal and postmenopausal women.J Ayub Coll Abbottabad 2015: 22(2): 143–145.
8. Bhattari T, Bhattacharya K, Chaudhuri P, Sengupta P. Correlation of common biochemical markers for bone turnover, serum calcium and alkaline phosphatase in postmenopausal women. Malays J Med Sci 2014; 21(1): 58–61.
9. Indumati V, Patil VS, Jailkhani R. Hospital Based Preliminary Study on Osteoporosis in Postmenopausal Women. Indian Journal of Clinical Biochemistry, 2007; 22(2): 96–100.
10. Sachdeva A, Seth S, Khosla AH, Sachdeva S. Study of some common biochemical bone turnover markers is postmenopausal women. Indian journal of clinical biochemistry 2005;20(1):131–134.
11. Sajjanar S, Sajjanar L. Study of serum alkaline phosphatase, calcium and urinary hydroxyproline as bone biomarkers in postmenopausal women. International journal of basic and applied medical sciences 2014;4(1):223–229.
12. Kumari N, Rosario B, Gowda KM. Altered liver function and the status of calcium in postmenopausal women in and around mangalore. Al Ameen J Med Sci 2010;3(2):115–119.
13. Vijayasree AP, Venkateswarlu K, Srirekha. Biochemical markers of bone turnover in pre & postmenopausal women. International journal of current medical and applied sciences 2015; 5(2);96–99.
14. Prabha S, Ashalata K, Babu PVS, Kumari PK and Nagamani M. A study of bone turnover markers (serum calcium, serum phosphorus and serum alkaline phosphatase) in postmenopausal women in east Godavari district, Andhra Pradesh, India. IOSR Journal of dental and medical sciences 2015; 14(6); 1–3.
15. Sri Rekha P, Venkateshwarlu U, Sarada U. Comparative study of biochemical bone turnover markers in pre & post-menopausal women. International journal of applied research 2015;1(5); 185–187.