Original Research Article

Serum Calcium and Alkaline Phosphatase Level among Pre-Menopausal and Post-Menopausal Women in Rupandehi District of Nepal: A Co-Relational Study

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ABSTRACT

Bone turnover markers and its consequence to poor health outcomes among post- menopausal women have been well understood elsewhere, but it is not well researched in Nepal.

Objective: This study is aimed to assess the association of bone turnover markers in pre- and post-menopausal women in Rupandehi district of Nepal.

Methods: A cross-sectional study was conducted during August 2014 to September 2016 in a total of 400 study participants with an equal number of pre- and post-menopausal women (200 each of the test and control group). Blood samples for both pre-menopausal and post-menopausal women were collected and analysed for the selected bone turnover markers. Descriptive statistics, bivariate and correlation statistics were employed for the study. Data were analysed using SPSS software version 20.

Results: This study identified that low serum calcium level. [(Post-menopausal; mean 8.53, SD 0.619 vs. pre menopausal; mean 9.23, SD 0.793) (P=0.000)] and high alkaline phosphatase (ALP) level in postmenopausal women compared to its counterparts [post-menopausal group 106.76 (SD 40.85) compared to the pre-menopausal group 85.20 (SD 31.262)]. There was a significant negative correlation between serum calcium and alkaline phosphatase.

Conclusion: As the result of this study showed a significant decrease in serum calcium and increase in serum ALP among normal postmenopausal women suggesting an elevated bone turnover may result into bone mass reduction, hormonal therapy to prevent bone mass reduction to concerned population may be suggested. Further, studies covering many bone markers in a large population are recommended.

Key words: Menopause, Osteoporosis, Serum calcium, Serum alkaline phosphatase

INTRODUCTION

Menopause is a condition in which there is permanent cessation of menses resulting from reduced ovarian hormone secretion that occurs naturally. Natural menopause is not associated with a pathologic cause and is recognized after 12 months of amenorrhea. [1]

Based on the menstrual bleeding patterns over the previous 12 months,

menopausal status is classified as premenopausal, at least 12 menses in the past 12 months with no change in regularity, perimenopausal, menses in the past 3 months with change in regularity, or 3 or more menses with change in regularity within the past 12 months and postmenopausal, no menses within the past 12 months. [2,3] Serum calcium and Alkaline Phosphatase (ALP) are the bone turnover markers which help in bone formation and mineralization. [4]

Osteoporosis is one of the most important public health problems in older adults and most common in post-menopausal life which not only gives rise to morbidity but also markedly reduces the quality of life in this population. [5] Menopause and ageing is known to associate with accelerated loss of cortical bone. Bone loss occurs when the balance between formation and resorption is upset and resorption is excessive resulting in a negative remodeling balance. [6]

A number of studies of bone turn over associated with disproportion of calcium and alkaline phosphatase (ALP) among postmenopausal women has been well documented. [7,8] For instances, a previously published paper revealed that menopausal and ageing altered the metabolism of serum calcium and ALP. [8]

Similarly, Bhattrai et al. reported the decreased level of serum calcium in postmenopausal women compared with premenopausal women and ALP level was found to be slightly higher among postmenopausal women; is key marker of bone mass reduction. [7]

A study from Nepal had also demonstrated the moderately reduced serum calcium in post-menopausal women and slightly increased serum ALP in early post-menopausal women. [9] However, the research related to calcium and alkaline phosphatase relationship and its poor outcome of bone pathology among post-menopausal is little understood in Nepal. With this current knowledge and understanding, the current study is aimed to assess the association of bone turnover markers in post-menopausal women in Rupandehi district of Nepal.

MATERIALS AND METHODS

This was the cross-sectional study performed during August 2014 to September 2016. The study setting was Devdaha medical College and Teaching Hospital. A total of 400 study participants were involved in this study with an equal number of pre- and post-menopausal women (200 each of the test and control group). Pre-menopausal women were of 14 to 40 years of age group while postmenopausal were of above 45 years of age. A sample size of 400 women were involved in the study based on the one of the study finding from Nepal that demonstrated the musculoskeletal problem of 27.3% in women above 40 years of age. [10] Exclusion criteria were Pregnancy, Smokers, Alcoholics and Oral contraceptives.

Sample collection

Blood samples for both Pre-menopausal and Post menopausal women were collected in a gel tube by vein puncture using 21SWG needles and syringes. Blood samples were allowed to clot and centrifuged at 3000 RPM for 10 minutes for proper separation of cells from serum and analysed within 24 hour of collection. Serum Calcium level was estimated using colorimetric method while alkaline phosphatase activity was determined using enzymatic methods by Earba Chem 5 V3 semi-automated chemistry analyzer. Other relevant data of subjects like age and menstrual cycle were recorded through comprehensive questionnaire.

Data were analysed using SPSS software version 20. Descriptive statistics such as Frequency, percentage, mean, standard deviation were employed in the study. Bivariate analyses were used to assess the association between serum calcium and alkaline phosphatase between

the test and control group. Additionally, persons' correlation test was also employed to assess the correlation between calcium and alkaline phosphate variation among the participants. The ethical committee of Devdaha Medical College & Teaching Hospital approved the study protocol. A written informed consent was obtained from each of the study participants and personal identifiers were removed before data analysis.

RESULT

Table 1 demonstrates the variations of calcium and alkaline phosphatase among

pre- and post-menopausal women. The statistical association was found with the reduced serum calcium levels among post-menopausal women compared to pre-menopausal women (Post-menopausal; mean 8.53, SD 0.619 vs. pre-menopausal; mean 9.23, SD 0.793, (P=0.000). However, serum calcium level in both group found to be within the normal reference range. Additionally, result of this study demonstrated that the serum ALP levels were significantly higher in (P = 0.000) in the post-menopausal group 106.76 (SD 40.85) compared to the pre-menopausal group 85.20 (SD 31.262).

Table 1. Differentials of calcium and alkaline phosphatase among pre- and post-menopausal women

Variables	Post-menopausal (n=200) (>45 years)				Pre-menopausal (n=200) (14-40 years)				t	p
	Minimum	Maximum	Mean	SD	Minimum	Maximum	Mean	SD		
Ca (mg/dl)	6	9	8.53	0.619	8	14	9.23	0.793	-9.381	0.000
ALP (U/L)	41	414	106.76	40.856	27	286	85.20	31.262	5.917	0.000

Fig. 1 shows a significant negative correlation between calcium and ALP (r = –0.147),
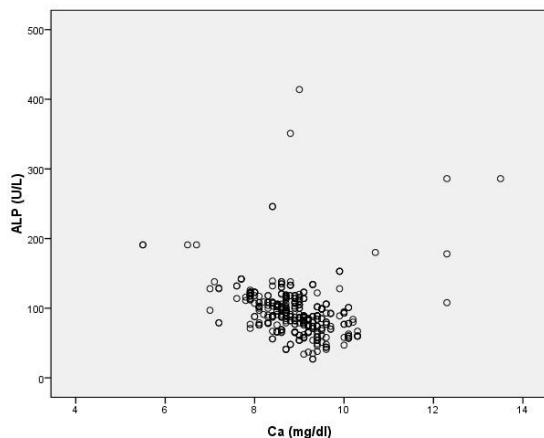Whereas serum ALP levels were elevated in post-menopausal women and serum calcium levels were decreased.

Fig. 1 Pearson correlation coefficient of serum calcium and serum ALP level in pre-menopausal and post menopausal women

DISCUSSION

Health and menopausal problems among post-menopausal women are numerous and draws the attention of health authority. [10] Bone turnover leading to poor health consequence is increasingly common in both developing and developed world.

[1,10,11] It is a dynamic process which increases at postmenopausal life as a consequence of estrogen deficiency. [12]

The current study identified that the changes in serum calcium level in both the test and control group. There was a statistically significant association with the reduced serum calcium levels among post-menopausal women compared to pre-menopausal women (Post-menopausal; mean 8.53, SD 0.619 vs. pre-menopausal; mean 9.23, SD 0.793) (P=0.000). On contrary to this, some studies reported that the serum calcium levels of post-menopausal women were significantly higher than those of pre-menopausal women. [8,13-15] However, this finding of our study is in the line of study performed by Bhale et al in an Indian study. [16]

The logic behind the increased serum calcium level could be reduction in bone mass and altered calcium metabolism due to decline in ovarian function. Estrogen deficiency that usually occurs among menopausal women may lead to calcium loss due to decreased intestinal calcium absorption and decreased renal calcium conservation. [17-19] Hormone and calcium therapy may be beneficial for menopausal women in this regard.

Additionally, result of this study demonstrated that the serum ALP levels were significantly higher in (P = 0.000) in the post-menopausal group 106.76 (SD 40.85) compared to the pre-menopausal group 85.20 (SD 31.262) which is consistent with the study of Onyeukwu et al. [8] and also accorded with Bhattrai et al. [7]

Many literatures demonstrated that estrogen deficiency which is common during menopause, induces synthesis of cytokines by osteoblasts, monocytes, and T cells and thereby stimulates bone resorption by increasing osteoclastic activity. This action could result in modification of the reabsorption, excretion, and resorption of calcium, which leads to increased circulating levels of this ion. [20-23]

Interestingly, this study showed a significant negative correlation between calcium and ALP (r = –0.147), whereas serum ALP levels were elevated in post-menopausal women and serum calcium levels were decreased which is similar to the study of Bhattrai et al. [7] Studies regarding the years since menopause found no significant correlation between serum calcium levels and ALP. [21] In contrast to the previous finding, higher levels of calcium and ALP have been demonstrated in postmenopausal women since ≤10 years of menopause compared with the postmenopausal women since ≥10 years of menopause. [24, 25]

This study has a number of strengths as it is based on primary data with possibly in a large sample size. To the best of researchers' knowledge none of the research has been performed and published in these areas from Nepal. Moreover, the change of bone turnover markers and its health consequence is one of the neglected issues in Nepal. Despite of these strengths, this study should be evaluated in the light of limitations. First, this study could not cover many other bone markers for example, inorganic phosphate, total protein, bone mineral density, vitamin D and hydroxyproline. Second, this study is limited to small area of Rupandehi district of Nepal. Further study covering larger area and many bone markers is recommended.

CONCLUSION

This study identified that there is a significant decrease in serum calcium and increase in serum ALP among normal postmenopausal women suggesting an elevated bone turnover may result into bone mass reduction. Additionally, there was negative correlation between serum calcium and serum ALP in postmenopausal women. Hormonal therapy to prevent bone mass reduction to concerned population may be suggested. Further, studies covering wide range of bone markers in a large population to support the generalizability of the study are recommended in coming days.

DISCLOSURE
The authors declared that they have no conflicts of interest in this study.

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