International Journal of Research in Medical Sciences
Kalita N et al. Int J Res Med Sci. 2017 May;5(5):1953-1958
www.msjonline.org
pISSN 2320-6071 | eISSN 2320-6012
DOI: http://dx.doi.org/10.18203/2320-6012.ijrms20171824

Original Research Article

A cross sectional study evaluating the association of serum calcium, serum magnesium, and body mass index in premenopausal and postmenopausal women

Neelakkhi Kalita*, Biju Dutta Choudhury

Department of Physiology, Gauhati Medical College, Guwahati, Assam, India

Received: 03 March 2017
Accepted: 31 March 2017

***Correspondence:**
Dr. Neelakkhi Kalita,
E-mail: neelakkhi@gmail.com

ABSTRACT

Background: To determine serum calcium, serum magnesium, and BMI (body mass index) in premenopausal and postmenopausal women, and find out any changes in these after menopause, and the independent association of serum calcium, serum magnesium with BMI in pre and post-menopausal women , if any.
Methods: 100 adult women attending Gauhati medical college outdoor clinics were included in the study. Patients with medical history of major systemic diseases, women on hormone replacement therapy, and women who had surgical menopause were not included in the study. Estimation of serum calcium and serum magnesium from cubital venous blood was done by photocolorimetry method. For statistical analysis the value of laboratory parameters were presented as the Mean±SD (standard deviation). A Student's unpaired t-test was used for cross-sectional comparisons of continuous variables between the groups.
Results: The mean serum calcium and also the mean serum magnesium levels were lower in the postmenopausal group and was statistically significant. Though the mean BMI in the postmenopausal group was higher than the premenopausal group, it was found to be statistically not significant.
Conclusions: The postmenopausal subjects had lower mean values of serum calcium and serum magnesium, but within the normal serum reference values.

Keywords: Body mass index, Premenopausal women, Postmenopausal women, Serum calcium, Serum magnesium

INTRODUCTION

Menopause is the consequence of exhaustion of the ovarian follicles which results in decreased production of female sex hormones.[1] The decrease in the level of sex steroid hormones during menopause in women causes various somatic, vasomotor, sexual and psychological symptom. The risk of osteoporosis, cardiovascular disease, arterial hypertension, impairment of glucose metabolism, and degenerative cognition disease incidence rises. The impact of deficiency of female sex hormones after menopause on the trace minerals has not been widely studied but expected menopause related changes in their status may have an impact on the above pathologies.

There are very few reports on the changes in serum calcium and magnesium levels in various phases of the menstrual cycle in otherwise healthy women. Estrogen induces hypercalcemia through the action of the parathyroid gland. Withdrawal of estrogen is reported to cause a significant loss of bone calcium. Increase in serum calcium levels during the follicular and ovulatory phases could be due to the effect of estrogen on the parathyroid glands.[2] In addition to bone calcium content the level of serum calcium appears to be associated with

blood pressure, and could be a metabolic risk factor for cardiovascular disease.[3]

Magnesium enhances bone turnover through the stimulation of osteoclastic function and its deficiency may play a role in postmenopausal osteoporosis. Magnesium acts as a surrogate for calcium in the transport and mineralization. Its deficiency may lead to disturbances in the cardiac rhythm, atheromatous plaques, raised cholesterol levels and a low value of HDL.[4] Magnesium plays a role in body temperature regulation. Heart palpitations associated with hot flushes as part of perimenopausal symptoms can also be improved by increasing intake of magnesium. Because Magnesium is present in most foods (legumes, vegetables, nuts, fruits, fish, dairy, grains etc.), severe magnesium deficiency should not occur in healthy people. Several studies have reported hypomagnesaemia in post menopausal women.

Significant decreases in the serum calcium and magnesium in the post menopausal women have been mentioned in studies with no significant difference in the BMI between postmenopausal and premenopausal women.[5] Obesity, having a high BMI ≥30 kg/m^2 is caused by several environment factors such as sedentary lifestyle and excessive energy intake. Studies have revealed that obesity can be due to abnormal calcium metabolism and a high calcium intake may prevent obesity.[6] Extracellular calcium ion concentration is determined by the interaction of calcium absorption from the intestine, renal excretion of calcium and bone uptake and release of calcium. Intracellular calcium plays a key role in modulating the factors involved in obesity.

PTH has a direct correlation with BMI since 25-OH vit. D is inversely related to PTH level. Activated Vit.-D (1,25, OH Vitamin D) elevates the calcium influx into adipocytes. Increased intracellular calcium increases lipid storage and also might activate phophodiesterase 3β which then reduces catecholamines induced lypolysis. Both these effects promote lipid storage in fat tissue. Estrogen reduces bone resorption by inhibiting interleukin IL-6 production and also controls the timing of osteoclast apoptosis. Thus bone turnover increases to high level in women soon after menopause. Thus it is of significant importance to compare serum levels of these micronutrients in women along with BMI so as to bring out any significant change in them individually with time elapsed since menopause, and advancing age, and also try to establish correlation among them, if any.

METHODS

The study was conducted in the Department of Physiology, Gauhati Medical College and Hospital during the period from July, 2015 to July, 2016, and was carried out on 100 adult women (premenopausal women: Normal healthy women of reproductive age group 20 to 44 years of age, Postmenopausal women: Normal, healthy women after attaining natural menopause, aged 45 to 75 years.) attending outpatient clinics. An informed consent was obtained from each patient prior to participation in the study. Patients with medical history of malignancy, tuberculosis, diabetes, thyroid, renal, rheumatoid and other endocrine diseases; patients who are taking medications known to affect body weight including HRT (Hormone Replacement Therapy) and women who had surgical menopause were not included in the study. The blood samples for analysis were collected between 8 AM and 9 AM after at least 8 hours of fasting. About 5 ml blood was drawn using dry and sterile disposable syringes from cubital vein. The serum obtained was collected in a centrifuge tube and centrifuged for 5 minutes at 3000 rpm.

The supernatant serum was transferred to a sterile container and stored at 2- 8^{O}C, or else used for immediate estimation of serum calcium and serum magnesium which was done by photocolorimetry method. For estimation of Body Mass Index (BMI= weight in kilogram/height in metre^2), weight was measured using a standard weighing machine. Height was recorded with the subject standing against a wall on which the tape was placed.

For statistical analysis the value of laboratory parameters were presented as the Mean±SD (standard deviation). A Student's unpaired t-test was used for cross-sectional comparisons of continuous variables between the groups. The results are considered statistically significant when the p value is <0.05. The main statistical comparisons were performed between the premenopausal and postmenopausal women.

RESULTS

The difference between post-menopausal (8.75±0.73mg/dl) and premenopausal mean serum calcium (9.46±0.60 mg/dl) was statistically significant (P<0.05).

Table 1: Mean Distribution of different parameters in postmenopausal group (n=50).

Parameter	Mean	SD	SE = SD/√n	95% C.I.
BMI (kg/m^2)	24.68	4.91	0.69	24.68±1.36
Serum Mg (mEq/L)	1.99	0.24	0.03	1.99±0.07
Serum Ca (mg/dl)	8.75	0.73	0.10	8.75±0.20

Table 2: Mean Distribution of different parameters in premenopausal group (n=50).

Parameter	Mean	SD	SE = SD/√n	95% C.I.
BMI (kg/m^2)	22.91	4.00	0.57	22.91±1.11
Serum Mg (mEq/L)	2.13	0.39	0.06	2.13±0.11
Serum Ca (mg/dl)	9.46	0.60	0.09	9.46±0.17

In the present study as compared to the premenopausal women (2.13mg/dl±0.39mg/dl), serum magnesium concentrations in postmenopausal women were low (1.99mg/dl±0.24mg/dl). Early postmenopausal women had serum magnesium levels (2.04mg/dl±0.24mg/dl) not significantly lower than the premenopausal group. In our series postmenopausal mean BMI (24.68 kg/m^2±4.91kg/m^2) was higher than the mean BMI(22.91 kg/m^2± 4.00 kg/m^2) of the premenopausal group but it was found to be statistically not significant.

DISCUSSION

Calcium ion is an essential structural component of the skeleton. Estrogen deficiency after menopause induces calcium loss by indirect effects on extra skeletal calcium homeostasis as well as decreased intestinal calcium absorption. When estrogen is deficient, there is an increase in the activation of new bone remodeling units. Both formation and resorption are altered with the result that resorption exceeds formation, producing a negative balance.[7] Estrogen deficiency may induce calcium loss due to decreased intestinal calcium absorption and decreased renal calcium conservation.[8,9]

The results of the present study indicated that the level of serum calcium declined significantly in post menopausal women. The similar results have been found in many other studies.[10-14]

Few studies observed a highly significant increase in the serum Ca levels after menopause, which according to them could be explained by estrogen deficiency, which induces synthesis of cytokine by the osteoblasts, monocytes and the T-cells, thereby increasing the stimulation of bone resorption by the increasing cytoclastic activity.[15,16] In elderly women, secondary hyperparathyroidism caused in part by reduced serum 25-hydroxy vitamin D appears to be a marginal determinant of an increased bone turnover rate.[17] Muneyyirci-Delale et al compared the Ca concentration in women of menopausal women in different phases of the menstrual cycle. Determination of the content of elements in serum reflect the concentration of extracellular fluid.[18] The fraction of extracellular Ca, which also includes functionally active ionized Ca exhibits greater sensitivity to changing hormonal profile. They showed that the average concentration of ionized Ca in the blood of postmenopausal women was significantly higher than in premenopausal women, regardless of the phase of the menstrual cycle.

Our study did not have an increase in the postmenopausal serum calcium in the early postmenopausal women less than 65 years of age. This finding may be explained by the following: increased requirement of calcium to maintain calcium homeostasis with advancing age, continued decline in intestinal calcium absorption reported with aging and the apparent loss of intestinal adaptation to varying calcium intake in older women.[19-21]

The variation of serum calcium with age is proposed to be explained by alterations in levels of serum albumin to which approximately 40% of circulating calcium is bound and which was not adjusted for the study along with the modification of the resorption, excretion and reabsorption of calcium**.** Studies have demonstrated that in addition to low estrogen levels, osteoporotic postmenopausal women had kidneys that did not reabsorb as much calcium as the kidneys of women without osteoporosis. Comparable to few other study series our study also had significantly reduced serum calcium in the postmenopausal group when compared to the premenopausal group ; however the serum calcium levels in both groups were within the normal reference range.[22,23] In Tromso survey of 27159 subjects it was found that mean serum calcium level was stable at a level of 2.35 mmol/L before menopause, and thereafter reached a plateau of 2.39 mmol/L[2].

Magnesium is the fourth most abundant cation in the body and the second most prevalent intracellular cation. Mg plays an essential role in more than 300 biological activities. Within the cell, Mg affects the function of organelles such as sarcoplasmic reticulum, primarily by its ability to alter Ca influx or mitochondria by altering their membrane's permeability to protons, which leads to alterations in the coupling of oxidative phosphorylation and electron transport chains, thus affecting the efficiency of ATP production. A decrease in serum Mg could decrease Mg levels inside the cells, which will lead to a decrease in Mg–ATP levels. The best recognized function of Mg is its association with ATP and the consequent facilitation of transphosphorylation reactions that are crucial to cell activation/deactivation as, for example, in signal transduction pathways. Most frequently, hypomagnesemia is an acquired disorder. Dietary Mg deficit is particularly important in older women where gastrointestinal and renal mechanisms for Mg conservation may be less efficient than in younger women. Mg depletion is frequently attributed to deregulation of factors controlling Mg metabolism and the reduction in the Mg exchange pools.

Many studies have found that serum magnesium level was significantly decreased in post menopausal than in pre menopausal females.[4,25]

The result of the present study is in accordance to the findings of these studies.

In the present study as compared to the premenopausal women, serum magnesium concentrations in postmenopausal women were low and decreasing with the time since the final menstruation similar to other series.[26] Reduced serum magnesium levels have attributed to the uncoupling of bone formation as a result of loss of the bone mass. It may also be related to urinary loss and is exacerbated by dietary element deprivation and gastrointestinal losses.[27] Renal Mg excretion increases in postmenopausal women, and is only reduced by the administration of hormone replacement therapy, which restores the levels of Mg to pre-menopause level.[27]

Although in the present study serum magnesium concentrations (1.99mg/dl±0.24mg/dl) in postmenopausal women were low and decreasing with the time since the final menstruation.

Several studies have reported an increase in the serum magnesium levels in postmenopausal women.[16,28,29]

The present result can be explained to be due to the uncoupling of bone formation as a result of loss of the bone mass in postmenopausal women. It may also be related to increased renal wasting and is exacerbated by dietary element deprivation and gastrointestinal losses.[30]

While a few studies on BMI changes as a function of the menopausal transition indicate that the observed changes are likely due to menopause, per se, most find that the commonly seen increase in BMI is probably more related to age increases than menstrual cessation.[18,19] Several cross-sectional studies using BMI found no significant difference with the menopause transition.

In our series the difference between mean BMI of postmenopausal and premenopausal women was not statistically significant, this is in accordance with several other studies.[5] Behavioral factors particularly exercises, were more strongly related to weight rather than menopause transition. Menopause is not associated with increases in BMI independent of normal aging.[31]

Whereas several other studies found a significant effect of menopause on BMI that appeared to be independent of age.[32-34] Because only moderate increases in total fatness have been found in postmenopausal women, discrepancies among the results may partially be explained by a lack of statistical power and also attributable to the fact that the effect of menopause on total body fatness may be transient.[32] Failure to control for the effects of age, and differences in diet or lifestyle (physical activity) in the experimental design also influenced the results.

Although BMI has been widely used as a screening tool for obesity, this index only represents a proxy measure of body fat mass, because it does not take into account differences in muscle and bone mass. Significant differences in BMI were noted between premenopausal and postmenopausal women in several studies.[32,35,36] The average differences in BMI between premenopausal and postmenopausal women are often small, thus making large samples necessary to detect these small differences. Because differences in BMI in these studies were found before adjustment for age, it is unclear whether these changes are independent of the aging process. Age-independent associations between menopausal status and BMI were found in several studies.[32,35] These reports found that BMI was higher in postmenopausal women after statistically adjusting for age.[35] It has been proposed that women who became postmenopausal had reductions in resting metabolic rate than women who remained premenopausal. These decreases in energy expenditure with no change or increases in energy intake will place women in positive energy balance, which will increase total fatness and possibly central adiposity. Potential mechanisms for the effects of menopause on energy regulation include possible effects of circulating estrogens and/or androgens on fat free mass and changes in food intake induced by estrogen deficiency on energy expenditure and physical activity levels remains unclear at present.[32]

Few studies are available evaluating the association of serum calcium, and serum magnesium with changes in BMI in the postmenopausal women.

R Jorde, et al did a health survey in 1994-95 in Tromso of 27159 subjects: Serum calcium showed a positive association with body mass index (BMI). The biological significance of the observed associations were mentioned as questionable.[24]

Song CH et al found that serum magnesium was inversely associated with body mass index (β=-0.283, P=0.001) and concluded that serum magnesium may be involved in the regulation of body size in adult women. They found no significant association of serum calcium with body weight and BMI.[37]

CONCLUSION

It was observed from the study that the mean serum calcium and also the mean serum magnesium levels were lower in the postmenopausal group, and the difference was statistically significant. Although the postmenopausal subjects had lower mean values of serum calcium and serum magnesium, still these were within the normal serum reference values as had been observed in

other studies. Though the mean BMI in the postmenopausal group was higher than the premenopausal group, it was statistically not significant.

We have used cross-sectional analyses to compare postmenopausal women with premenopausal women. Although cross-sectional investigations may provide clues regarding the effects of the menopause on the physiological and biochemical changes, confounding factors such as age, ethnicity, average energy intake, physical activity, serum albumin levels etc., have to be adjusted for statistical procedures to find out the changes in the variables independent of these factors.

The present study revealed that the differences between the mean values and standard deviations of the variables in the premenopausal and postmenopausal groups were small; thus making large samples necessary to detect these differences.

Our premenopausal group included few perimenopausal subjects also. Thus in order to establish standard reference values and formulate predictive equations, a representation of the whole population needs to be studied. Further large scale multicentric and longitudinal studies are required to further determine the actual changes in BMI, serum levels of magnesium and calcium, and correlation or independent association between them for their clinical implications in various disorders with transition of age, and passage of menopause which is inevitable in every woman's life.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Sachdeva A, Seth S, Khosla AH, Sachdeva S. Study of some common biochemical bone turn over markers in post menopausal women. Indian J Biochemistry. 2005;20(1):131-4.
2. Pitkin RM, Reynolds WA. Williams GA, Hargis GK. Calcium regulating hormones during the menstrual cycle. J Clin Endocrinol Metabol. 1978:47:626-32.
3. Fujita T. Calcium paradox: consequences of calcium deficiency manifested by a wide variety of diseases. J Bone Miner Metab. 2000;18:234-6.
4. Anke M. Role of trace elements of in the dynamics of arteriosclerosis. Z Gesamte Inn Med. 1986;41(4):105-11.
5. Jandial S, Kaur G, Kumar S, Choudhary PR. Study of Serum Calcium and Magnesium Levels in Post Menopausal Women. The Indian J Nutrition and Dietetics. 2014;51(1):76-81.
6. Henry RP, Davies KM, Barger–Lux MJ. Calcium and weight clinical studies. J American College of Nutrition. 2002;21(2):152S-5S.
7. Kumar SKH. Bhaskar P. Osteoporosis an emerging disease of the 21st century. J Fam Med Prim Care. 2012:66-6.
8. Uebelhart D, Schlemmer A, Johansen JS, Gineyts E, Christiansen C, Delmas PD. Effect of menopause and hormone replacement therapy on the urinary excretion of pyridinium cross-links. J Clin Endocrinal Metab. 1991;72:367-73
9. Christiansen C, Delmas PD. Effect of menopause and hormone replacement therapy on the urinary excretion of pyridinium cross-links. J Clin Endocrinol Metab. 1991;72:367-73.
10. Bhale DV, Ansari HA. Study of serum calcium levels in postmenopausal women of Aurangabad district. International J Recent Trends in Science an Technology. 2014;9(3):332-3.
11. Indumati V, Patil VS, Jailkhan R. Hospital based preliminary study on osteoporosis in postmenopausal women. Indian J clinical Biochemistry. 2007;22(2):96-100.
12. Khatake PD, Jadhav SS, Afroz S. Relation between serum calcium level, bone mineral density and blood pressure in post menopausal women. International Journal of Recent Trends in Science and Technology.2013;7(3):86-8.
13. Qureshi HJ, Hussain G, Jafary ZA, Bashir MU, Latif N, Riaz Z. Calcium status in premenopausal and postmenopausal women. J Ayub Med Coll Abbottabad. 2010;22(2):143-5.
14. Gallagher JC, Kinyamu HK, Fowler SE, Dawson-Hughes B, Dalsky GP, Sherman SS. Calciotropic hormones and bone markers in the elderly. Journal of Bone and Mineral Research. 1998;13(3):475-82.
15. Gupta N, Arora KS. Trace elements after menopause: A comparative study. J Clinical and Diagnostic Reserarch. 2011;5(4):795-7.
16. Hodgekinson A. Plasma electrolyte concentrations in women and the effect of estrogen administration. Maturitas. 1982;4:247-56.
17. Riggs BL, Arnaud CD, Jowsey J, Goldsmith RS, Kelly PJ. Parathyroid function in primary osteoporosis. Journal of Clinical Investigation. 1973;52(1):181.
18. Muneyyirci-Delale O, Nacharaju VL, Dalloul M, Altura BM, Altura BT. Serum ionized magnesium and calcium in women after menopause: inverse relation of estrogen with ionized magnesium. Fertility and sterility. 1999;71(5):869-72.
19. Heany RP, Recker RR, Sarille PD. Menopausal changes in calcium balance performance. J Lab Clin Med. 1978;92:953.
20. Ireland P, Fordtrans JS. Effect of dietary calcium and age on jejunal calcium absorption in humans studied by intestinal perfusion. J Clin Invest. 1973;52:2672.
21. Gallagher JC, Riggs BL, Eisman J, Hamstra A, Arnaud SB, DeLuca HF. Intestinal calcium absorption and serum vitamin D metabolites in normal subjects and osteoporotic patients: effect of

age and dietary calcium. J Clin Invest. 1979;64(3):729-36.
22. Ilich JZ, Brownbill RA, Tamborini L. Bone and nutrition in elderly women: protein, energy, and calcium as main determinants of bone mineral density. Eu J of Clin Nutr. 2003;57:554-65.
23. Bhattarai T, Bhattacharya K, Chaudhuri P, Sengupta P. Correlation of common biochemical markers for bone turnover, serum calcium, and alkaline phosphatase in post-menopausal women. The Malaysian J Medical Sciences. 2014;21(1):58.
24. Jorde R, Sundsfjord J, Bønaa KH. Determinants of serum calcium in men and women. The Tromsø Study. Eur J Epidemiol. 2001;17(12):1117-23.
25. Saltman PD, Strause LG. The role of trace minerals in osteoporosis. J Am Nutr. 1993;12:384-9.
26. Grochans E, Karakiewicz B, Kozielec T, Brodowska A, Brodowski J, Starczewski A, et al. Serum Mg and Zn levels in postmenopausal women. Magnesium research. 2012;24(4):209-14.
27. McNair P, Christiansen C, Transbol I. Effect of menopause and estrogen substitutional therapy on magnesium metabolism. Miner Electrol Metab. 1984;10:84-7.
28. Lindsay R, Hart DM, Ferrest C. Effect of a natural and artificial menopause on serum, urinary and erythrocyte magnesium. Clin Sci. 1980;58:255-7.
29. Stanton MF, Lowenstein FW. Serum magnesium in women during pregnancy, while taking contraceptives, and after menopause. J Am Coll Nutr. 1987;6(4):313-9.
30. Mutlu M, Argun M, Kilic E, Saraymen R, Yazar S. Magnesium, zinc and copper status in osteoporotic, osteopenic and normal postmenopausal women. J International Medical Research. 2007;35:692-5.
31. Crawford SL, Casey VA, Avis NE, McKinlay SM. A longitudinal study of weight and the menopause transition: results from the Massachusetts Women's Health Study. Menopause. 2000;7(2):96-104.
32. Pasquali R, Casimirri LF, Labate AM, Tortelli O, Pascal G, Anconetani B, et al. Body weight, fat distribution and the menopausal status in women. Maturitas. 1995;3(21):259.
33. Pasquali R, Vicennati V, Bertazzo D, Casimirri F, Pascal G, Tortelli O, Labate AM. Determinants of sex hormone—binding globulin blood concentrations in premenopausal and postmenopausal women with different estrogen status. Metabolism. 1997;46(1):5-9.
34. den Tonkelaar I, Seidell JC, van Noord PA, Baanders-van Halewijn EA, Ouwehand IJ. Fat distribution in relation to age, degree of obesity, smoking habits, parity and estrogen use: a cross-sectional study in 11825 Dutch women participating in the DOM-project. Int J Obes. 1990;14:753-61.
35. Tonkelaar ID, Seidell JC, Van Noord PA, Baanders-van Halewijn EA, Jacobus JH, Bruning PF. Factors influencing waist/hip ratio in randomly selected pre- and post-menopausal women in the dom-project (preliminary results). International J obesity. 1988;13(6):817-24.
36. Ley CJ, Lees B, Stevenson JC. Sex- and menopause associated changes in body-fat distribution. Am J Clin Nutr. 1992;55:950-4
37. Song CH, Choi WS, Kim KS. Associations of serum minerals with body mass index in adult women. European J Clinical Nutrition. 2007;61:682-5.

Cite this article as: Kalita N, Choudhury BD. A cross sectional study evaluating the association of serum calcium, serum magnesium, and body mass index in premenopausal and postmenopausal women. Int J Res Med Sci 2017;5:1953-8.