

## Research Article

# A comparative study of serum calcium, magnesium and its ratio in women of menopausal and reproductive age group

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**Received:** 10 June 2015

**Accepted:** 26 June 2015

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### ABSTRACT

**Background:** The menstrual cycle is the result of complex interacting processes within the hypothalamus, the hypophysis, the ovaries and the uterus. Patterns of change in plasma concentrations of various minerals have been the subject of several research endeavours. Therefore, the present study has been conducted to study and compare the serum calcium, magnesium and its ratio in menopausal and reproductive age group.

**Methods:** The study was performed in two groups of subjects with a control group of 30 healthy women of reproductive age group and a postmenopausal group of 30 women with varying durations of menopause (less than and more than 10 years after menopause). Three blood samples were obtained from the control group –one each in early follicular phase, ovulatory phase and during luteal phase for estimation of calcium and magnesium. One sample was taken from the menopausal age group for the estimation of calcium and magnesium using commercially available kit. The values are expressed as mean  $\pm$  S.D. The comparison between the different phases of menstrual cycle in reproductive age group with menopausal women was performed using student t-test. P value less than 0.05 was considered significant.

**Result:** The serum  $\text{Ca}^{2+}$ ,  $\text{Mg}^{2+}$  and Calcium/ Magnesium ratio was found to be statistically insignificant ( $p=1.00$ ), during different phases of menstrual cycle in normal cycling women is statistically insignificant.

**Discussion:** The cyclical changes of serum  $\text{Ca}^{2+}$  and Serum  $\text{Mg}^{2+}$  levels in women of reproductive age may be due to the cyclical changes in the level of sex hormones during different phases of menstrual cycle.

**Keywords:** Serum  $\text{Ca}^{2+}$ , Serum  $\text{Mg}^{2+}$ ,  $\text{Ca}^{2+}/\text{Mg}^{2+}$  ratio, Women of reproductive age

### INTRODUCTION

Epidemiological evidences are accumulating to indicate that certain essential minerals may serve physiological roles in regulating the biological activity in females during menstrual cycle. Patterns of change in plasma concentrations of various minerals have been the subject of several research endeavours to delineate the association between hormonal changes and essential minerals.

In women, the internal milieu undergoes relatively rapid physiological changes at puberty and at climacteric.

Menarche and menopause are the two landmarks of the female life cycle.<sup>1</sup> The changes in the ovarian function account for these events. The menstrual cycle is the result of complex interacting processes within the hypothalamus, the hypophysis, the ovaries and the uterus. Patterns of change in plasma concentrations of various minerals have been the subject of several research endeavors.<sup>2</sup>

The role of divalent cations  $\text{Ca}^{2+}$  and  $\text{Mg}^{2+}$  have been implicated in premenstrual syndromes in general.<sup>1</sup> Conditions like premenstrual migraine, preeclampsia, eclampsia, menopausal cardiovascular risk, bone

problems and the adverse effects after the use of oral contraceptives and hormone replacement therapy are some of the conditions influenced by the divalent cations. Both ions are involved in intermediary metabolism, neuromuscular activity, excitation secretion coupling, cardiovascular health and bone metabolism and also in all those activities and entities that are regulated by various hormones, including sex steroids as well.<sup>3</sup>

Numerous studies were performed to delineate the association between changes in the plasma levels of female sex hormones estrogen and progesterone with the plasma levels of divalent cations, Ca<sup>2+</sup> and Mg<sup>2+</sup>. Therefore, the present study has been conducted to study and compare the serum calcium, magnesium and its ratio in menopausal and reproductive age group.

**METHODS**

The present study was undertaken to study the serum concentrations of divalent cations Ca<sup>2+</sup> and Mg<sup>2+</sup> in normal healthy menopausal women and in healthy women of reproductive age group. This was performed after the institutional ethical clearance. The study was performed in two groups of subjects with a control group of 30 healthy women of reproductive age group and a postmenopausal group of 30 women with varying durations of menopause (less than and more than 10 years after menopause).

**Selection of Subjects**

The control group consists of 30 healthy women of reproductive age group (25-30 and 30-35 years). The study group consists of 30 menopausal women of different age groups with varying durations of menopause. The women on hormonal treatment and those with history of diabetes, hypertension, or systemic illnesses were excluded from the study. A prior written informed consent was obtained from all the subjects.

**Collection of Blood Samples**

Disposable syringes and needles were used to collect blood samples from the subjects. Under all aseptic precautions, 5 ml of blood was drawn from antecubital vein and was collected in two clean dry bottles. The 28 - 29 day menstrual cycle was divided into 5 day menstruation, 8 day follicular phase, 6 day ovulatory period, and a 10 day luteal phase.<sup>4</sup> Three blood samples were obtained from the control group –one each in early follicular phase, ovulatory phase and during luteal phase for estimation of calcium and magnesium. One sample was taken from the menopausal age group for the estimation of calcium and magnesium.

Serum ionized calcium was calculated from the formula:

$$\text{Serum ionised Ca (mg \%)} = \frac{6 \times \text{total Ca (mg \%)} - \text{K}/3}{\text{K} + 3}$$

Where K is total protein in g%

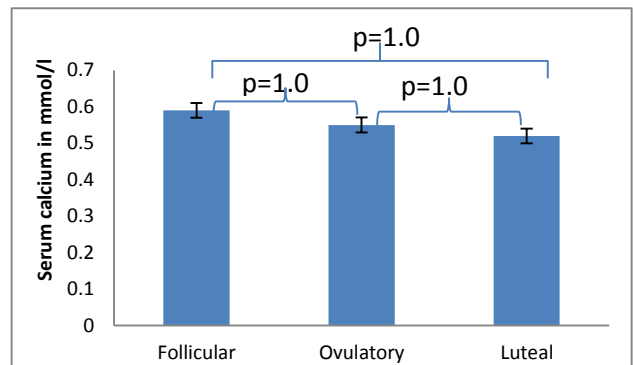
Total magnesium was assayed calorimetrically. Ionised magnesium was obtained by calculation. It corresponds to 60% of total magnesium.

**Statistical Analysis**

The values are expressed as mean ± S.D. The comparison between the different phases of menstrual cycle in reproductive age group with menopausal women was performed using student t test. P value less than 0.05 was considered significant.

**RESULTS**

In the present study, the mean values of calcium (mmol/l) during follicular, ovulatory, luteal phases of menstrual cycle were represented in Figure 1 and Table 1-3. No statistically significant cyclical changes of serum Ca<sup>2+</sup> were observed (p=1.00), during different phases of menstrual cycle in normal cycling women, but the highest levels were seen during the luteal phase.



**Figure 1: Comparison of serum calcium (mmol/l) during various phases of menstrual cycle in women of reproductive age. The p value between follicular & ovulatory, follicular & luteal and ovulatory & luteal phase is 1.0 which is non-significant.**

**Table 1: Comparison of serum calcium (mmol/l) levels in the follicular phase of women of reproductive age and menopausal women.**

	Menopausal subjects	Follicular Phase of Subjects of reproductive age
Mean	1.14	1.17
Standard Deviation	0.7	0.1
P value	0.8	

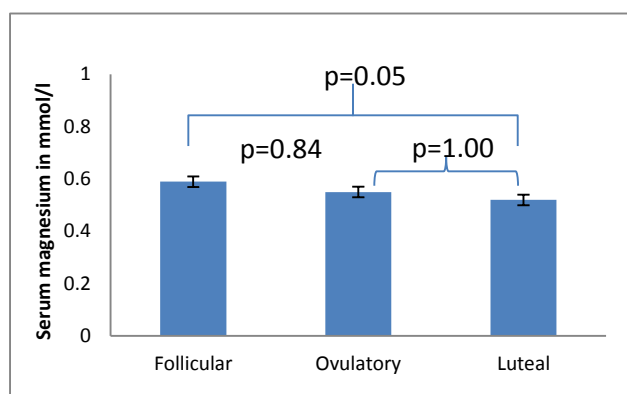
**Table 2: Comparison of serum calcium (mmol/l) levels in the ovulatory phase of women of reproductive age and menopausal women.**

	Menopausal subjects	Ovulatory Phase of Subjects of reproductive age
Mean	1.14	1.16
Standard Deviation	0.7	0.06
P value	1.00	

**Table 3: Comparison of serum calcium (mmol/l) levels in the luteal phase of women of reproductive age and menopausal women.**

	Menopausal subjects	Luteal Phase of Subjects of reproductive age
Mean	1.14	1.16
Standard Deviation	0.7	0.06
P value	1.00	

The mean values of magnesium (mmol/l) during follicular, ovulatory, luteal phases of menstrual cycle were represented in Figure 2 and Table 4-6. Serum Mg<sup>2+</sup> levels in women of reproductive age showed cyclical fluctuations during the menstrual cycle, with the highest levels being in the follicular phase. Serum Mg<sup>2+</sup> levels were higher in the menopausal women than normal cycling women during their ovulatory and luteal phase. No significant difference was seen between the values in menopausal women and in follicular phase.



**Figure 2: Comparison of serum magnesium (mmol/l) during various phases of menstrual cycle in women of reproductive age. The p value between follicular & ovulatory, follicular & luteal and ovulatory & luteal phase are 0.84, 0.05 and 1.0 respectively.**

Comparison of serum Calcium/ Magnesium ratio in the follicular, ovulatory and luteal phase of women of reproductive age and menopausal women was performed and shown in Table 7-9. The Calcium/ Magnesium ratio

was found to be statistically not significant in the follicular phase whereas, it was found to be statistically significant during the ovulatory phase (p=0.04) and also during the luteal phase (p=0.01). Healthy women of reproductive age group demonstrated cyclical changes of ionised magnesium and Ca<sup>2+</sup>/Mg<sup>2+</sup> ratio. The Ca<sup>2+</sup>/Mg<sup>2+</sup> ratio was lowest in women after menopause.

**Table 4: Comparison of serum magnesium (mmol/l) levels in the follicular phase of women of reproductive age and menopausal women.**

	Menopausal subjects	Follicular Phase of Subjects of reproductive age
Mean	0.6	0.59
Standard Deviation	0.08	0.1
P value	1.00	

**Table 5: Comparison of serum magnesium (mmol/l) levels in the ovulatory phase of menopausal women with the women of reproductive age.**

	Menopausal subjects	Ovulatory Phase of Subjects of reproductive age
Mean	1.14	0.55
Standard Deviation	0.7	0.11
P value	0.3	

**Table 6: Comparison of serum magnesium (mmol/l) levels in the luteal phase of women of reproductive age and menopausal women.**

	Menopausal subjects	Luteal Phase of Subjects of reproductive age
Mean	1.14	0.52
Standard Deviation	0.7	0.11
P value	0.01	

**Table 7: Comparison of serum calcium/ magnesium ratio in the follicular phase of women of reproductive age and menopausal women.**

	Menopausal subjects	Follicular Phase of Subjects of reproductive age
Mean	1.86	2.02
Standard Deviation	0.42	0.42
P value	0.96	

**Table 8: Comparison of serum calcium/ magnesium ratio in the ovulatory phase of women of reproductive age and menopausal women.**

	Menopausal subjects	Ovulatory Phase of Subjects of reproductive age
Mean	1.86	2.18
Standard Deviation	0.42	0.48
P value	0.04	

**Table 9: Comparison of serum calcium/ magnesium ratio in the luteal phase of women of reproductive age and menopausal women.**

	Menopausal subjects	Luteal Phase of Subjects of reproductive age
Mean	1.86	2.31
Standard Deviation	0.42	0.5
P value	0.01	

## DISCUSSION

The present study was conducted to compare the levels of divalent cations in normal healthy menopausal women and in healthy women of reproductive age group. The study was performed in two groups of subjects: a control group of 30 healthy women of reproductive age group and a postmenopausal group of 30 women with varying durations of menopause (less than and more than 10 years after menopause).

In the present study, no statistically significant cyclical changes of serum  $Ca^{2+}$  were observed, during different phases of menstrual cycle in normal cycling women, but the highest levels were seen during the luteal phase. The Serum  $Mg^{2+}$  levels in women of reproductive age showed cyclical fluctuations during the menstrual cycle, with the highest levels being in the follicular phase. Serum  $Mg^{2+}$  levels were higher in the menopausal women than normal cycling women during their ovulatory and luteal phase. No significant difference was seen between the values in menopausal women and in follicular phase. These variations may be due to the cyclical changes in the level of sex hormones during different phases of menstrual cycle.

Many researchers observed similar cyclical fluctuations of divalent cations throughout the menstrual cycle. In the study conducted by Muneyyirci et al. in normal women, it was observed that the serum levels of divalent cations  $Ca^{2+}$  and  $Mg^{2+}$  showed cyclical fluctuation in a cycle along with the levels of estrogen and progesterone<sup>5</sup>. There were corresponding variations in the  $Ca^{2+}/Mg^{2+}$  ratio as well. During the early follicular phase, levels of  $Mg^{2+}$  were comparatively elevated and the level of  $Ca^{2+}$

was comparatively low. As the estrogen level rises and reaches ovulatory values, the  $Mg^{2+}$  levels fell and  $Ca^{2+}$  level rose. When the level of progesterone peaked, the levels of  $Mg^{2+}$  were low, the  $Ca^{2+}$  levels rose and the ratio of  $Ca^{2+}$  to  $Mg^{2+}$  was significantly increased<sup>4</sup>.

Muneyyirci et al. in normal women observed that the serum  $Mg^{2+}$  showed cyclical fluctuation in a cycle along with the levels of estrogen and progesterone.<sup>5</sup> During the early follicular phase, levels of  $Mg^{2+}$  were comparatively elevated. As the estrogen level rises and reaches ovulatory.

Values, the  $Mg^{2+}$  levels fell. When the level of progesterone peaked, the level of  $Mg^{2+}$  was low. During menopause, the levels of estrogen and progesterone were very low. In menopausal women the levels of  $Mg^{2+}$  were sufficiently higher than the levels seen in normal cycling women. It was concluded that  $Mg^{2+}$  level was inversely and significantly related to serum estrogen levels in menopausal women and in reproductive age group. Muneyyirci et al, Pandya et al, Das k et al observed that magnesium levels were lowest at the time of ovulation when the estrogen levels peaked.<sup>5-7</sup> The interrelationship of magnesium with estrogen was studied extensively by Seelig et al. and hypothesized that estrogen induced shifts of magnesium can be deleterious when estrogen levels are high and magnesium intake is low.<sup>8</sup>

It has been well documented that during the menopausal stage of a women's life, bone metabolism is increased to a point where breakdown is more prevalent than build up. Serum  $Ca^{2+}$  levels typically rise with the cessation of menstrual function. This is due to an increased propensity to osteoporosis in the menopausal women. It was found that in menopausal women, mean levels of  $Mg^{2+}$  and total Mg were similar to that seen during the early follicular phase of the healthy cycling women. During this phase the estrogen and progesterone levels were comparatively low in the healthy women. The level of  $Mg^{2+}$  was sufficiently higher than the levels seen in healthy cycling women during high estrogen phase (ovulatory phase). Muneyyirci et al. had reported that that  $Mg^{2+}$  level was inversely and significantly related to serum estrogen levels in healthy cycling women and menopausal women.<sup>5</sup> In menopausal and postmenopausal women mean levels of  $Mg^{2+}$  and total magnesium were similar to those in cycling women during the early follicular phase, when estrogen and progesterone levels are comparatively low.<sup>4</sup>

### Calcium Magnesium Ratio

Delale et al. observed a significant increase in  $Ca^{2+}/Mg^{2+}$  ratio during the peak of estrogen and progesterone secretion.<sup>5</sup> The fact that the  $Ca^{2+}/Mg^{2+}$  ratio was increased simultaneously with the peak of estrogen and progesterone confirms that its effect is present throughout premenstrual period and suggests that this ratio may be related to premenstrual syndrome

complaints which many women have.<sup>9</sup> It is demonstrated recently by many investigators that this ratio is associated with onset of migraine and tension headaches. Many clinical trials also indicate that these headaches are relieved in most women after IV administration of Mg. It has been shown repeatedly that this ratio is important in blood vessel tone, excitation secretion coupling, synaptic transmission and bone metabolism.<sup>10</sup>

*Conflict of interest: None declared*

*Funding: ICMR-STC funding*

*Ethical approval: The study was approved by the Institutional Ethics Committee*

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**Cite this article as:** Sukumaran S. A comparative study of serum calcium, magnesium and its ratio in women of menopausal and reproductive age group. *Int J Res Med Sci* 2015;3(8):2024-8.