

## SERUM INORGANIC PHOSPHORUS, URIC ACID, CALCIUM, MAGNESIUM AND SODIUM STATUS DURING UTERINE CHANGES OF MENSTRUAL CYCLE

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### ABSTRACT

**Objectives:** The present study was undertaken to determine the changes in levels of serum inorganic phosphorus, uric acid, calcium, magnesium and sodium during uterine changes of menstrual cycle.

**Material & Methods:** Forty healthy menstruating regularly women, around 18-34 years of age, participated as subjects in our study. Estimation of serum inorganic phosphorus, uric acid, calcium, and magnesium were done by UV Molybdate (End point assay), Modified Trinder Peroxidase method, O-Cresolphthalein-Complexone method, and Calmagite method. Sodium levels were analyzed by Neochem Sodium-Potassium kit (Colorimetric and Turbidimetric Method).

**Results:** The mean serum inorganic phosphorous level in menstrual Phase ( $4.11 \pm 0.40$ ) was significantly higher as compared to proliferative Phase ( $3.64 \pm 0.44$ ) and secretory Phase ( $3.23 \pm 0.54$ ). The levels of serum uric acid were significantly decreased ( $p < 0.05$ ) in secretory Phase whereas serum calcium level was increased in the proliferative Phase. The serum magnesium level was significantly decreased from menstrual to proliferative Phase ( $p < 0.05$ ), thereafter it again rose. The levels of serum sodium were significantly decreased in secretory Phase as compared to other two Phases of the cycle.

**Conclusions:** Alternation of serum inorganic phosphorous, uric acid, calcium, magnesium and sodium levels were noted during uterine changes of menstrual cycle, however, none of all the mention levels were outside the physiological limits.

**Keywords:** Inorganic phosphorous, Uric acid, Calcium, Magnesium, Sodium, Menstrual Cycle.

### 1. Introduction

The menstrual cycle is the scientific term for the physiological changes that can occur in fertile female humans and apes<sup>1</sup>. It is defined as the cyclic event that takes place in a rhythmic fashion during the reproductive period of a woman's life. The onset of menstrual cycle usually occurring between 12 to 15 years, called menarche and the termination of menstrual cycle at the age of 45 to 50 years is called menopause<sup>2</sup>. The average menstrual cycle is 28 days long from the first day of one menstrual period to the first day of the next<sup>3</sup>. A normal menstrual cycle is typically between 21 and 35 days between menstrual periods<sup>4</sup>. During each menstrual cycle, along with ovarian changes, uterine changes also occur simultaneously. The changes in uterus take place in three Phases: Menstrual Phase, Proliferative Phase and Secretory Phase<sup>2</sup>. In Menstrual Phase, regular menstruation or eumenorrhoea (the process of shedding and exit of uterine lining along with blood and fluids) lasts for a few days, usually 3 to 5 days, but anywhere from 2 to 8 days is considered normal<sup>5</sup>. The average volume of menstrual fluid during a monthly menstrual period is 35

milliliters. Menstrual fluid is reddish-brown in color and it contains some blood, as well as cervical mucus, vaginal secretions, and endometrial tissue<sup>2, 4</sup>. During menstrual Phase, there is a lack of estrogen and progesterone hormones which, causes involution of endometrium and release of vasoconstrictor substances like prostaglandins. Prostaglandin's produces vasoconstriction lead to hypoxia, which results in the necrosis of the endometrium and rupturing of blood vessels and blood oozes out along with necrotic endometrium<sup>2,6-8</sup>. Proliferative Phase extends usually from 5<sup>th</sup> to 14<sup>th</sup> day of menstruation. It corresponds to the follicular Phase of ovarian cycle, during which there is an increase of 1-5 mm in the endometrium. Uterine changes during proliferative Phase occur because of the influence of estrogens release from ovary<sup>2, 9</sup>. The secretory Phase extends between 15<sup>th</sup> and 28<sup>th</sup> day of the menstrual cycle, i.e. between the day of ovulation and the day when menstruation of next cycle commences. It corresponds to the luteal Phase of ovarian cycle. During secretory Phase large quantity of progesterone and small amount of estrogen are secreted by corpus

luteum. Progesterone causing coiling of the endometrial vessels and a thickening of the endometrium<sup>2</sup>.

Many women reports retention of fluid during the premenstrual days, especially noting breast swelling and abdominal bloating<sup>10</sup>. Possible causes for this claim of many women could be due to change in sodium concentration includes the increased concentrations of antidiuretic hormone in the luteal Phase<sup>11</sup> and the antagonism effect of progesterone to the typical sodium retentive influence of aldosterone<sup>12</sup>. The concentration of uric acid in plasma increases after menopause. This is believed to be the result from decrease in sex-steroid concentration, similar to that which occurs at the time of onset of menstruation<sup>13</sup>.

It is possible that changes in hormone concentrations during the uterine change of menstrual cycle may influence the concentrations in serum of commonly measured analytes. Hence, the purpose of this study was to estimate serum levels of inorganic phosphorus, uric acid, calcium, magnesium and sodium levels during uterine changes of menstrual cycle.

## 2. Material and Methods

The study was conducted in the department of Biochemistry, Rohilkhand Medical College and Hospital, Bareilly from August 2011 to March 2012. The study included forty healthy menstruating regularly women, around 18-34 years of age with cycle length between 25 to 35 days. Subjects using hormonal methods of contraception, having history of any significant illness affecting the menstrual cycle and subjects taking any medication (including dietary supplements such as vitamins) for at least a month before the study were excluded.

Each subjects was explained the aim and the method of the test to eliminate fear and apprehension, as per ethical committee clearance guidelines dictated by the college. 5 ml venous blood was drawn during each Phase of cycle i.e. during the menstrual Phase (within the first 2 days of the cycle), during the proliferative Phase (8th to 14th days) and during the secretory Phase (after the 22nd day of the cycle) until the next cycle began. Estimation of serum inorganic phosphorus, uric acid, calcium, and magnesium were done by UV Molybdate (End point assay)<sup>14</sup>, Modified Trinder Peroxidase method<sup>15</sup>, O-Cresolphthalein-Complexone method<sup>16</sup> and Calmagite method<sup>17</sup>. Sodium levels were analyzed by Neochem Sodium-Potassium kit (Colorimetric Method)<sup>18</sup>.

Statistical analysis of the data was carried out by ANOVA Test.

## 3. Results

Table-1 and 2, Fig-1, 2 and 3 shows our results. The mean age of subjects was  $23.5 \pm 4.04$  years (18-34 years). The duration of the menstrual cycle varied from 25 days to 35 days with a mean  $\pm$  SD of  $29.4 \pm 2.8$  days, while the duration of menstrual Phase varied from 2 to 8 days (Table-1).

Gradual decrease in serum inorganic phosphorus levels were seen from menstrual Phase to proliferative Phase and from the proliferative Phase to secretory Phase. The levels of serum uric acid were significantly ( $p < 0.05$ ) decreased in secretory Phase. In the proliferative Phase, serum calcium levels were significantly higher as compare to the other two Phases. The serum magnesium levels significantly decreased from menstrual to proliferative Phase, thereafter it again rose. The levels of serum sodium were significantly decreased in secretory Phase as compared to other two Phases of cycle. However, none of all the mention values were outside the normal range.

## 3. Discussion

There are scanty reports on the changes in the levels of serum inorganic phosphorous, uric acid, calcium, magnesium and sodium in various Phases of the menstrual cycle. . The cyclic hormonal changes can affect a variety of physiological and biochemical processes. Changes in these analytes are, however, reported to be mainly due to changes in the hormonal levels during the different Phases of the menstrual cycle<sup>19, 20</sup>.

On analyzing the results of our study, we observed that the values of serum inorganic phosphorus were significantly low in proliferative Phase and secretory Phase as compared to menstrual Phase of the cycle. A number of observations reported similar type of significant changes of serum inorganic phosphorus values during the different Phases of the menstrual cycle<sup>21-23</sup>. During proliferative Phase and secretory Phase serum inorganic phosphorus values were low could be due to estrogen. High estrogen production can lead to increase in parathyroid activity which further causes fall in phosphate concentration rapidly than the calcium rise. The decline in phosphate concentration could be caused by strong effect of parathyroid hormone on kidney resulting in excessive renal phosphate excretion<sup>22, 24</sup>. In this

present study the mean level of serum uric acid during secretory Phase ( $4.2 \pm 1.19$ ) was significantly low in comparison to other two Phases as shown in Table-2, Fig.-1. The results are in agreement with the results obtained by Lanje *et al.*<sup>23</sup>. The change in uric acid concentration in present study parallels that seen after menopause. During the luteal Phase the concentration of ovarian steroids in the circulation is high and the uric acid concentration is low, whereas in the proliferative Phase or follicular Phase the reverse is true<sup>24</sup>.

The present study also revealed that the mean levels of serum calcium ( $10.02 \pm 0.78$ ) were significantly higher in proliferative Phase or follicular Phase as compared to the other two Phases. These results agree with previous findings of some workers<sup>25, 26</sup>. In 1978 Pitkin RM *et al.* reported, higher serum calcium levels during proliferative Phase could be due to the effect of estrogen on the parathyroid glands<sup>27</sup>. But during the secretory Phase or luteal Phase serum calcium levels were low, could be due to higher levels of progesterone compared to estrogen, as reported by Christiansen C *et al* in his study<sup>28</sup>.

In our study it was found that the levels of serum magnesium were significantly decreased from menstrual to proliferative Phase, thereafter it again rose (Table-2; Fig-2). Similar results were also observed by other authors [22, 25]. The raised estrogen levels possibly by acting through parathyroid hormone could be responsible for depicting the body stores of magnesium by decreasing the reabsorption of magnesium ions by the renal tubules thus resulting in midcycle decline<sup>29</sup>.

In Table-2, Fig.-3, it has also been observed that the values of sodium in serum were significantly decreased during secretory Phase or luteal Phase of the cycle. Similar finding were observed by Dr. M.A. Lanje *et al.* and M. Mira *et al.*<sup>30,31</sup>. Possible causes for this change in sodium concentration includes the increased concentrations of antidiuretic hormone in the luteal Phase<sup>32</sup> or of other steroid hormones or metabolites that were not measured in this study. This change in plasma sodium supports the claim of many women that they suffer changes in fluid balance in the premenstrual days<sup>31</sup>.

### Conclusion

These cyclical changes in inorganic phosphorus, uric acid, calcium, magnesium and sodium levels in serum supports the claim of many women that they suffer changes in fluid and

electrolyte balance in the premenstrual days. We were able to reduce the sign and symptoms in them with the use of magnesium infusion or its salts along with vitamin D during secretory Phase or luteal Phase as suggested by Mauskop *et al.*<sup>33</sup>.

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**Table-1 Showing the Age Distribution and Duration of the Menstrual Cycle and Menstrual Phase**

Age in years	Mean age of 40 subjects	Duration of Menstrual Cycle	Mean Menstrual Cycle	Duration Menstrual Phase
18-34 years	23.5 ± 4.04	25-35 days	29.4 ± 2.8 days	2 to 8 days

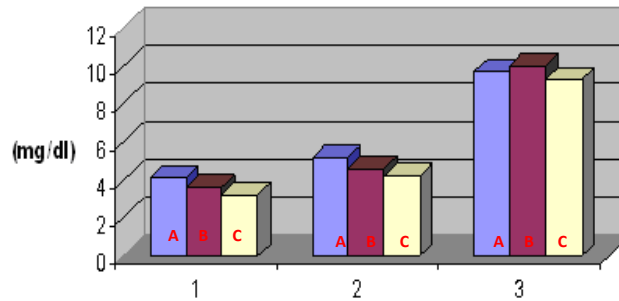
**Table 2 The Mean Values of Serum Inorganic Phosphorus, Uric Acid, Calcium, Magnesium and Sodium during Uterine Changes of Menstrual Cycle**

Analytes	Normal Range	Menstrual Phase	Proliferative Phase	Secretory Phase
Inorganic Phosphorus (mg/dl)	2.5-4.5	4.11± 0.40▼	3.64 ±0.44	3.23 ±0.543
Uric Acid (mg/dl)	2.5-6.2	5.17 ± 1.08	4.6 ± 1.26	4.2 ± 1.19 #
Calcium (mg/dl)	8.5-10.5	9.71±0.814	10.02 ± 0.78▼	9.30±0.38
Magnesium (meq/l)	1.4-1.9	1.86±.078	1.77±0.14#	1.80±0.12
Sodium (mmol/l)	135-155	148.72±5.6	145.87 ± 6.2	143.42±6.2#

n=40; ▼significantly higher as compared to the other two Phases (P < 0.05)

# significantly lowers as compared to the other two Phases (P < 0.05)

**Figure-1 Showing Relationship between Serum Inorganic Phosphorus, Uric Acid and Calcium during Uterine Change of Menstrual Cycle**



**1. Inorganic Phosphorus,**

- A)Menstrual Phase =4.11± 0.40
- B)Proliferative Phase=3.64 ±0.44
- C)Secretory Phase= 3.23 ±0.54

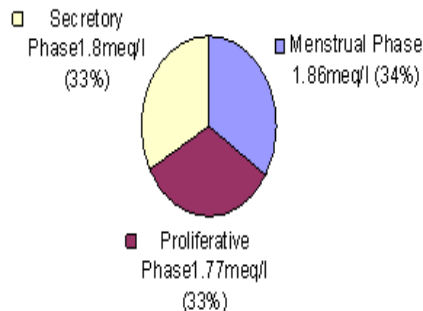
**2. Uric Acid,**

- A)Menstrual Phase=5.17 ± 1.08
- B)Proliferative Phase=4.6 ± 1.26
- C)Secretory Phase=4.2 ± 1.19

**3. Calcium**

- A)Menstrual Phase= 9.71±0.814
- B)Proliferative Phase=10.02 ± 0.7
- C) Secretory Phase= 9.30±0.38

**Figure-2 Showing the mean Serum Magnesium levels in meq/l during Uterine Change of Menstrual Cycle**



**Figures-3 Showing the mean Serum Sodium levels in mmol/l during Uterine Change of Menstrual Cycle**

