

## Parasympathetic Nerve Function Status During Different Phases Of Menstrual Cycle In Healthy Young Women

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### Abstract

**Background:** Autonomic nerve function status may be changed during follicular and late luteal phases of menstrual cycle due to fluctuations of serum estrogen and progesterone levels. This alteration in autonomic nerve functions may affect cardiovascular control and usually associated with decreased parasympathetic activity in late luteal phase. **Objective:** To observe the parasympathetic nerve function status during follicular and late luteal phases of menstrual cycle and also their relationships with serum estrogen and progesterone levels in healthy young women. **Methods:** This cross-sectional study was carried out in the Department of Physiology, Sir Salimullah Medical College (SSMC), Dhaka from 1<sup>st</sup> January 2009 to 31<sup>st</sup> December 2009. A total number of thirty (30) apparently healthy unmarried women age ranged from 20-25 years were studied in both follicular (phase A, control) and late luteal (phase B, study) phases of menstrual cycle. Simple autonomic nerve function tests like heart rate (HR) response to valsalva maneuver (Valsalva ratio), HR response to deep breathing, HR response to standing (30<sup>th</sup>:15<sup>th</sup> ratio) were done to assess parasympathetic activity and serum estrogen and progesterone levels were also measured by AxSYM method. All these tests were performed in both follicular and late luteal phases of menstrual cycle of the same subject. Data were analysed by paired student's 't' test and Pearson's correlation coefficient test as applicable. **Results:** Mean values of both HR response to Valsalva ratio and HR response to standing (30<sup>th</sup>:15<sup>th</sup>) were non-significantly decreased but HR response to deep breathing was significantly ( $p < 0.05$ ) decreased in late luteal phase than those of follicular phase. **Conclusion:** From this study it can be concluded that parasympathetic activity is decreased in late luteal phase of menstrual cycle.

**Key words:** Parasympathetic nerve functions, progesterone, menstrual cycle

J Bangladesh Soc Physiol. 2011 December; 6(2): 100-107  
For Authors Affiliation, see end of text.

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### Introduction

Regular menstrual cycle is an index of women's normal reproductive health. It includes follicular phase and luteal phase<sup>1</sup>. The biological rhythmicity of the cycle is created by the interplay among hypothalamic, hypophyseal and ovarian hormones<sup>2</sup>. The fluctuations in hormonal levels affect not only the female reproductive tract but also many other tissues of the body. Variations in the autonomic

nerve function status may also be related to these fluctuations<sup>3</sup>. Some women during reproductive years may experience some physical, psychological and behavioral symptoms which occur in late luteal phase of menstrual cycle termed as premenstrual syndrome (PMS) and in severe case termed as premenstrual dysphoric disorder (PMDD)<sup>4</sup>. However, altered functioning of autonomic nervous system in late luteal phase may be responsible for this PMS or in severe case PMDD in eumenorrhic women. Alterations in

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Received August 2011; Accepted November 2011

autonomic nerve functions may affect cardiac-vagal control and usually associated with decreased parasympathetic activity in late luteal phase<sup>5</sup>.

Five simple non-invasive cardiovascular reflex tests have been considered to evaluate the status of cardiovascular autonomic nerve control<sup>6</sup>. These tests include, heart rate (HR) response to valsalva maneuver (Valsalva ratio), HR response to deep breathing, HR response to standing (30<sup>th</sup>:15<sup>th</sup> ratio) for evaluation of cardiac parasympathetic activity.

Significantly increased value of Valsalva ratio was observed during preovulatory phase in comparison to early follicular and midluteal phases in some eumenorrhic women<sup>7</sup>. However, this ratio was found to increase significantly during luteal phase than that of follicular phase<sup>8</sup>. On the contrary, no significant changes of HR response to Valsalva maneuver, HR response to deep breathing and HR response to standing i.e. 30<sup>th</sup>:15<sup>th</sup> ratio during different phases of menstrual cycle were also reported<sup>9</sup>.

A study on Heart Rate Variability (HRV) by power spectral analysis found predominant parasympathetic activity in follicular phase than that of luteal phase<sup>10</sup>. In another study parasympathetic nerve activity was increased in follicular phase and sympathetic activity was predominant in luteal phase<sup>11</sup>. Again, a significant increased value of resting heart rate at ovulation with no change of HRV in different phases of menstrual cycle was also reported by some other investigators<sup>12</sup>.

However, female are engaged in different types of productive activity. Their health care is very important to give birth of healthy population and also for their efficient work. To the best of our knowledge very little is known about parasympathetic nerve function status in healthy young women in Bangladesh. Therefore, the present study was undertaken to create awareness among the healthy young women to

improve the quality of life and also the physicians to take appropriate measure for prevention of complications.

### Methods

The present cross-sectional study was carried out in the Department of Physiology, SSMC, Dhaka from 1<sup>st</sup> January 2009 to 31<sup>st</sup> December 2009. In this study, a total number of 30 apparently healthy women age ranged from 20-25 years with regular menstrual cycle were studied in both follicular (Phase A-control) and late luteal phases (Phase B-study) of menstrual cycle. All the subjects were selected from the medical students of SSMC belonged to middle socioeconomic status. Subjects with diabetes mellitus, hypertension, cardiac diseases, chronic obstructive lung disease, history of neurological problem, chronic renal failure, using prescribed medicine, having any acute or chronic disease were excluded from this study. By conventional method, parasympathetic nerve function tests and serum estrogen and progesterone levels of all the subjects were studied in both phases.

The purpose and procedure of the study were explained to each subject. Written informed consent was taken from all the participants. Study protocol was approved by Institutional Ethics Committee (IEC) of Sir Salimullah Medical College (SSMC), Dhaka. Detailed medical and family history was recorded in a prefixed questionnaire. Height and weight of the subjects were recorded and BMI was calculated. Under aseptic precaution 5 ml of venous blood was collected and serum was prepared for estimation of serum estrogen and progesterone level by AxSYM method<sup>13</sup>. For assessment of parasympathetic nerve function, some non-invasive cardiovascular reflex tests were done in the Department of Physiology of SSMC. These tests include heart rate response to Valsalva maneuver (Valsalva ratio), heart rate response to deep breathing, heart rate response to standing

(30<sup>th</sup> : 15<sup>th</sup> ratio)<sup>6</sup>. Before the tests, all the subjects took rest in supine position for 15 minutes. Resting heart rate and resting systolic and diastolic blood pressure of all subjects were also recorded.

Statistical analysis of data was done by using SPSS program version-15. All the data were expressed as Mean  $\pm$  SD (standard deviation) and was analyzed by paired Student's 't' test and Pearson's correlation coefficient test as applicable.

### Results

Anthropometric data of the subjects are expressed in Table I.

**Table I :** Age and BMI in young healthy women (n=30)

Variables	Values
Age (in year)	21.57 $\pm$ 1.30(20-25)
BMI (kg/m <sup>2</sup> )	20.68 $\pm$ 0.99 (18.99-22.77)

Figures in parentheses indicate ranges.

Resting heart rate and blood pressure of the subjects are given in Table II. All the values are within reference range. So, the subjects are normotensive with normal heart rate.

The mean values of HR response to valsalva maneuver (valsalva ratio) and HR response to standing (30<sup>th</sup>: 15<sup>th</sup> ratio) both were non-significantly decreased. Whereas, HR response to deep breathing (maximum – minimum HR) was significantly ( $p < 0.05$ ) decreased in late luteal phase (Phase B) than those of follicular phase (Phase A). (Table-III).

The mean value of estrogen was increased in late luteal phase (Phase B) than that of in follicular phase (Phase A). But it was not statistically significant. Again, the mean progesterone level in late luteal phase (Phase B) was significantly ( $p < 0.001$ ) increased than that of follicular phase (Phase A) (Table IV).

Valsalva ratio and Heart rate response to deep breathing both were negatively correlated but heart rate response to standing was positively correlated with serum estrogen level in follicular phase (Phase A) and in late luteal phase (Phase

**Table II:** Resting heart rate and blood pressure of young healthy women in both phases of menstrual cycle (n=30)

Variables	Phase A	Phase B	p value
Resting heart rate (beats/min)	72.20 $\pm$ 4.96 (64-80)	73.73 $\pm$ 3.87 (66-84)	0.007**
Resting blood pressure: Systolic (mm of Hg)	109.97 $\pm$ 6.52 (100-120)	111.93 $\pm$ 4.99 (100-120)	0.027*
Resting blood pressure: Diastolic (mm of Hg)	67.67 $\pm$ 5.37 (60-80)	68.40 $\pm$ 5.34 (60-80)	0.125 <sup>ns</sup>

Data are expressed as mean  $\pm$  SD. Figures in parentheses indicate ranges.

Statistical analysis was done by paired t test.

Phase A = Follicular phase (Control group)

Phase B = Late luteal phase (Study group)

\* = Significant at  $p < 0.05$

\*\*= Significant at  $p < 0.01$

ns = Not significant

n= Total number of subjects

**Table III :** Parasympathetic nerve function status of young healthy women in both phases of menstrual cycle (n=30)

Heart rate response to	Phase A	Phase B	p value
Valsalva ratio	1.40±0.15 (1.21-1.77)	1.39±0.15 (1.20-1.71)	0.620 <sup>ns</sup>
Deep breathing (beats/min)	31.70±6.06 (18.32-47.40)	30.15±6.32 (15.23-40.05)	0.031*
30 <sup>th</sup> :15 <sup>th</sup>	1.11±0.05 (1.06-1.26)	1.10±0.03 (1.07-1.17)	0.399 <sup>ns</sup>

**Table IV :** Serum estrogen and progesterone levels of young healthy women in both phases of menstrual cycle (n=30)

Variables	Phase A	Phase B	p value
Serum estrogen (pgm/dl)	108.83±61.33 (44-289)	122.33±48.27 (51-246)	0.323 <sup>ns</sup>
Serum progesterone (ng/dl)	0.90±0.34 (0.50-2.09)	13.49±6.69 (6.00-32.68)	0.001***

Data are expressed as mean ± SD, Figures in parentheses indicate ranges.

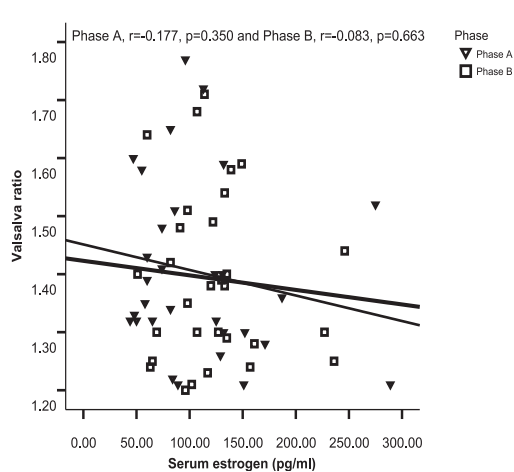
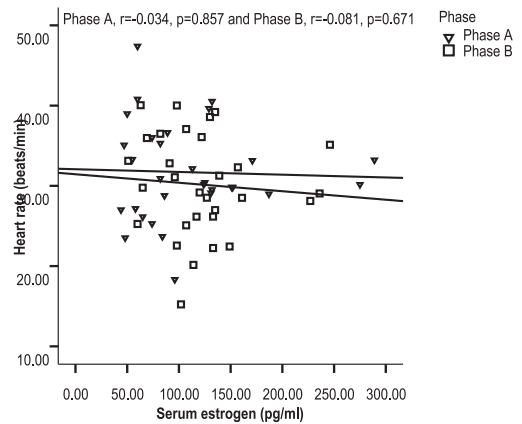
Phase A =Follicular phase (Control group), Phase B = Late luteal phase (Study group)

\*\*\*=Significant at p <0.001, ns = Not significant

B). But the relationships were not statistically significant (Figure 1, 2 and 3).

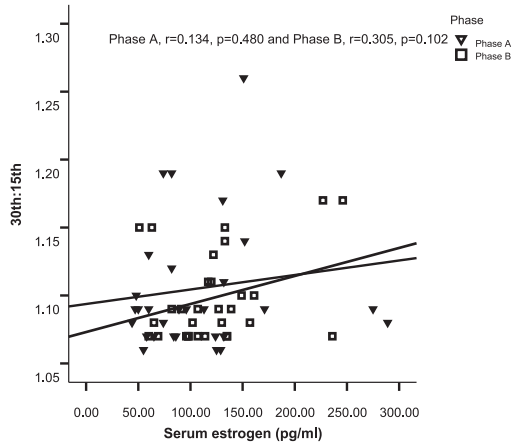
Again, valsalva ratio was negatively correlated but heart rate response to deep breathing and

heart rate response to standing were positively correlated with serum progesterone level in late luteal phase (Phase B). However, the relationships were not statistically significant (Figure 4, 5 and 6).

**Figure 1:** Correlation of serum estrogen level with valsalva ratio in both phases of menstrual cycle (n=30)**Figure 2:** Correlation of serum estrogen level with heart rate response to deep breathing in both phases of menstrual cycle (n=30)

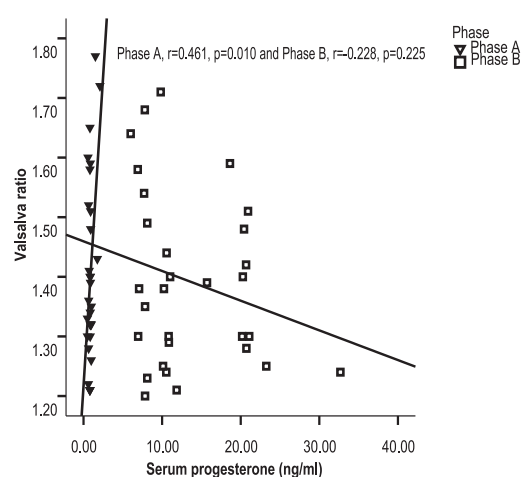
Phase A =Follicular phase (Control)

Phase B = Late luteal phase (Study), ns= not significant

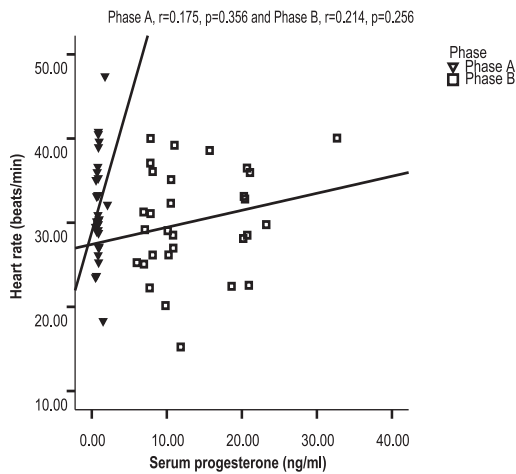


**Figure 3 :** Correlation of serum estrogen level with heart rate response to standing in both phases of menstrual cycle (n=30)

Phase A =Follicular phase (Control), Phase B = Late luteal phase (Study), \*=Significant at  $p < 0.05$ , ns= not significant

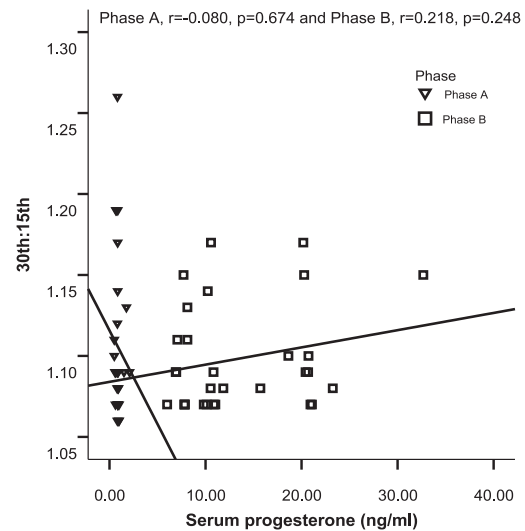


**Figure 4 :** Correlation of serum progesterone level with valsalva ratio in both phases of menstrual cycle (n=30)



**Figure 5 :** Correlation of serum progesterone level with heart rate response to deep breathing in both phases of menstrual cycle (n=30)

Phase A =Follicular phase (Control), Phase B = Late luteal phase (Study), ns= not significant



**Figure 6 :** Correlation of serum progesterone level with heart rate response to standing in both phases of menstrual cycle (n=30)

### Discussion

In the present study, significantly decreased value of HR response to deep breathing (maximum – minimum HR) and non-significant decreased value of both HR response to valsalva maneuver (Valsalva ratio) and HR response to standing (30<sup>th</sup>: 15<sup>th</sup> ratio) were observed in late luteal phase in comparison to those of follicular phase, indicate decreased parasympathetic activity in this phase in healthy young women. This is further strengthened by decreased value of resting heart rate and blood pressure during this phase. Similar results were observed by some other investigators but they have used spectral analysis of HRV<sup>14,15</sup>. On the contrary, other researchers didn't find any significant change of parasympathetic activities during different phases of menstrual cycle in some eumenorrhic women<sup>9</sup>.

Furthermore, serum estrogen level was non-significantly and serum progesterone level was significantly increased in late luteal phase than those of follicular phase. Similar observations were also made by some other research workers<sup>8,10</sup>. However, serum estrogen showed non-significant negative correlation with Valsalva ratio and HR response to deep breathing but positive correlation with HR response to standing during both phases of menstrual cycle. Again, serum progesterone was negatively correlated with Valsalva ratio but positively correlated with HR response to deep breathing and HR response to standing during late luteal phase of menstrual cycle. All these correlations were statistically non-significant. No data are available for comparison.

Different investigators have suggested some mechanisms responsible for decreased parasympathetic activity in late luteal phase of menstrual cycle. In follicular phase, the enhanced parasympathetic activity may be due to increased estrogen level<sup>10,11,16</sup>. In follicular phase, estrogen increases density as well as the function of presynaptic  $\alpha_2$  adrenoreceptors thereby

resulting in significant decrease in nor-epinephrine induced responses<sup>17</sup>. Estrogen stimulates the opening of calcium activated potassium channels by nitric oxide<sup>18</sup>. Estrogen also stimulates opening of calcium activated potassium channels by cyclic guanosine monophosphate dependent pathway<sup>19</sup>. Thus estrogen relaxes vascular smooth muscle and promoting vasodilatation. Again, estradiol might be associated with increase in acetylcholine concentration<sup>20</sup>. These findings suggested that, estrogen has facilitating effect on cardio-vagal function<sup>21</sup>.

On the contrary, decreased parasympathetic activity in late luteal phase might be due to increased level of progesterone during this phase. It has been suggested that, progesterone inhibits the influence of estrogen on cardio-vagal activity<sup>22</sup>. Again, Progesterone may increase cardiac excitability by its opposing effects on estrogen<sup>20</sup>. It has also been reported that estradiol increases the number and sensitivity of progesterone receptor, thus increasing action of progesterone hormone during luteal phase. Again, progesterone exerts inhibitory effect on the cariovagal baroreflex responses<sup>7</sup>.

In the present study, fluctuation of estrogen and progesterone levels may be responsible for the changes in parasympathetic activity in follicular and late luteal phases of menstrual cycle. However, increased parasympathetic activity during follicular phase might be due to the influence of estrogenic effect. Positive correlation of estrogen with heart rate response to standing in follicular phase is in favor of this statement. Again, decreased parasympathetic activities in late luteal phase may be due to increased level of progesterone. Negative correlation of progesterone with Valsalva ratio in luteal phase also supports this finding.

### Conclusion

From the result of the study, it can be concluded that parasympathetic activity was decreased in



late luteal phase in comparison to follicular phase of menstrual cycle.

### Acknowledgement

Authors of this study acknowledge the partial financial support from the research grant of DGHS of Bangladesh. The authors are also thankful to the study subjects for their active and enthusiastic participation.

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