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CARDIOVASCULAR AUTONOMIC FUNCTION ACROSS DIFFERENT PHASES OF THE MENSTRUAL CYCLE IN HEALTHY YOUNG WOMEN

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ABSTRACT

The menstrual cycle is associated with cyclical fluctuations in ovarian hormones that influence cardiovascular autonomic regulation. This study evaluated cardiovascular autonomic function across the menstrual, follicular, and luteal phases of the menstrual cycle in healthy young women. An observational cross-sectional study was conducted among 105 healthy female medical students aged 18–21 years with regular menstrual cycles. Cardiovascular autonomic function was assessed using standardized autonomic function tests, including Resting Heart Rate, Resting Blood Pressure, 30:15 Ratio, Expiration–Inspiration (E:I) Ratio, Standing–Lying Ratio, Supine–Standing Blood Pressure Response, and the Cold Pressor Test. Statistical analysis was performed to compare autonomic parameters across the three menstrual phases, with a significance level of $p < 0.05$. Resting heart rate, diastolic blood pressure, and diastolic responses to the Supine–Standing test and Cold Pressor Test were significantly higher during the luteal phase, indicating greater sympathetic activity. In contrast, the 30:15 ratio and E:I ratio were significantly higher during the follicular phase, reflecting enhanced parasympathetic modulation. The findings demonstrate significant phase-dependent variations in cardiovascular autonomic function, highlighting the influence of ovarian hormones on autonomic regulation and emphasizing the importance of considering menstrual phase during cardiovascular autonomic assessment in women.

Keywords: Menstrual cycle, Cardiovascular autonomic function, Parasympathetic activity, Sympathetic activity, Ovarian hormones.

INTRODUCTION

The menstrual cycle is a normal physiological process regulated by cyclical fluctuations in the ovarian hormones estrogen and progesterone.[1] The average menstrual cycle lasts approximately 28 days and consists of the menstrual, follicular, ovulatory, and luteal phases, each characterized by distinct hormonal changes.[2] These cyclic hormonal fluctuations regulate reproductive function and also influence several organ systems, including the cardiovascular, nervous, endocrine, and renal systems.[3]

The autonomic nervous system (ANS) is responsible for maintaining cardiovascular homeostasis by regulating heart rate, blood pressure, myocardial contractility, and vascular tone through coordinated sympathetic and parasympathetic activity.[1] Estrogen exerts cardioprotective effects by enhancing parasympathetic activity, improving endothelial function, and increasing nitric oxide-mediated vasodilation.[4] Progesterone has been associated with relatively increased sympathetic activity, greater peripheral vascular resistance, and altered cardiovascular regulation during the luteal phase.[1] Because of these hormonal influences, cardiovascular autonomic function may vary during different phases of the menstrual cycle.[3]

Cardiovascular autonomic function can be evaluated using standardized non-invasive autonomic function tests that assess sympathetic and parasympathetic activity.[5] Commonly used parasympathetic function tests include resting heart rate, heart rate response to standing (30:15 ratio), Expiration–Inspiration (E:I)

ratio, and Standing–Lying ratio, whereas sympathetic function can be assessed using resting blood pressure, blood pressure response to standing, and the Cold Pressor Test.[5] Several investigators have evaluated cardiovascular autonomic function during different phases of the menstrual cycle; however, their findings remain inconsistent. Yazar and Yazıcı reported increased sympathetic activity with reduced parasympathetic modulation during the luteal phase.[6] Similarly, Yildirir et al. observed reduced vagal activity during the luteal phase using heart rate variability analysis.[7] Bai et al. also demonstrated greater sympathetic predominance during the luteal phase based on nonlinear heart rate variability analysis.[8] Matsumoto et al. reported increased autonomic nervous system activity during the late luteal phase in women with premenstrual symptoms.[9]

In contrast, Fuenmayor et al. observed relatively greater parasympathetic influence during the luteal phase.[10] Chung and Yang reported variations in heart rate variability across the menstrual cycle, suggesting increased sympathetic modulation during the follicular phase in shift-work nurses.[11] Priyadharshini et al. demonstrated significantly greater cardiovagal activity during the follicular phase.[12] Verma et al. similarly reported enhanced parasympathetic function during the follicular phase using conventional autonomic function tests.[13] Parlewar and Venkatraman also found significantly greater parasympathetic activity during the follicular phase.[14] Patra et al. recently confirmed increased parasympathetic autonomic function during the follicular phase among healthy young women.[15]

Other investigators, including Mehta and Chakrabarty, Christina et al., Saeki et al., Leicht et al., Schmalenberger et al., and Rani and Venkatesh, have likewise demonstrated menstrual cycle-related variations in autonomic function, although the magnitude and direction of these changes have varied between studies.[16,17,18,19,20,21]

The variability among previous studies may be attributed to differences in study design, sample size, methods used for determining menstrual phase, hormonal assessment, and the autonomic function tests employed.[4]

Although numerous studies have investigated autonomic regulation during the menstrual cycle, relatively few have comprehensively evaluated both sympathetic and parasympathetic cardiovascular autonomic functions using a complete battery of standardized autonomic function tests in healthy young Indian women.[22]

Therefore, the present study was undertaken to evaluate cardiovascular autonomic function across the menstrual, follicular, and luteal phases of the menstrual cycle in healthy young women using standardized cardiovascular autonomic function tests. The findings may contribute to a better understanding of physiological autonomic adaptations during the menstrual cycle and improve the interpretation of cardiovascular autonomic function tests in women of reproductive age.

MATERIALS AND METHODS

Study Design

This observational cross-sectional study was conducted in the Department of Physiology, Bidar Institute of Medical Sciences (BRIMS), Bidar, Karnataka, India, over a period of one year. The study was designed to evaluate cardiovascular autonomic function during different phases of the menstrual cycle in healthy young women.

Study Population

A total of **105 healthy female medical students** aged **18–21 years** with regular menstrual cycles were enrolled in the study after obtaining written informed consent.

Inclusion Criteria

Participants fulfilling the following criteria were included:

- Healthy female medical students aged 18–21 years.
- Regular menstrual cycles of 27–30 days.
- Normotensive and non-obese.
- Eumenorrheic, unmarried, and nulliparous.
- Willing to participate and provide written informed consent.

Exclusion Criteria

Participants with any of the following were excluded:

- Irregular menstrual cycles or pregnancy.
- History of hypertension, diabetes mellitus, thyroid disorders, cardiovascular disease, or other systemic illnesses.
- Acute illness at the time of the study.
- History of smoking or alcohol consumption.
- Use of oral contraceptive pills or medications affecting autonomic function or hormonal status.

Study Procedure

Baseline demographic and anthropometric data, including age, height, weight, and body mass index (BMI), were recorded for all participants. Cardiovascular autonomic function tests were performed during three phases of a single menstrual cycle:

- **Menstrual phase:** Days 1–5
- **Follicular phase:** Days 6–14
- **Luteal phase:** Days 15–28

All recordings were carried out between **9:00 AM and 11:00 AM** in a quiet laboratory under standardized environmental conditions. Participants were instructed to avoid caffeine, strenuous physical activity, and heavy meals for at least one hour before testing and were allowed to rest for 30 minutes before the recordings.

Cardiovascular Autonomic Function Tests

Cardiovascular autonomic function was assessed using a **digital physiograph (Physio-Pac,**

Medicaid Systems) following standard laboratory procedures.

Parasympathetic Function Tests

- Resting Heart Rate (RHR)
- Heart Rate Response to Standing (30:15 Ratio)
- Expiration: Inspiration (E:I) Ratio
- Standing: Lying (S:L) Ratio

Sympathetic Function Tests

- Resting Blood Pressure (RBP)
- Blood Pressure Response to Standing (Supine–Standing Test)
- Cold Pressor Test (CPT)

Statistical Analysis

The collected data were entered into Microsoft Excel and analyzed using IBM SPSS Statistics version 18.0. Continuous variables were expressed as mean ± standard deviation (SD). Comparisons of autonomic function parameters across the menstrual, follicular, and luteal phases were performed using one-way Analysis of Variance (ANOVA) followed by Bonferroni post hoc analysis for pairwise comparisons. A p-value < 0.05 was considered statistically significant.

Ethical Considerations

The study was approved by the Institutional Ethics Committee of Bidar Institute of Medical Sciences, Bidar (Approval No.: 217/BRIMS/IEC/2023). Written informed consent was obtained from all participants before enrollment. Confidentiality of participant information was maintained throughout the study, and the study was conducted in accordance with the ethical principles of the Declaration of Helsinki.

RESULTS

A total of 105 healthy female medical students aged 18–21 years completed the study. The mean age of the participants was 18.81 ± 0.81 years, and the mean body mass index (BMI) was 22.22 ± 2.69 kg/m². The baseline characteristics of the study participants are presented in Table 1.

Table 1: The mean of age and BMI

	N	Mean	Std. Deviation	Std. Error	Range	Minimum	Maximum
Age (yrs)	105	18.81	0.81	0.08	3	18	21
BMI (Kg/m2)	105	22.22	2.69	0.26	14.9	14.3	29.2

The comparison of cardiovascular autonomic function parameters across the menstrual, follicular, and luteal phases is presented in **Table 2**.

Table 2: Comparison of Cardiovascular Autonomic Function Parameters Across Different Phases of the Menstrual Cycle

AFT Parameters	MP Mean ± SD	FP Mean ± SD	LP Mean ± SD	F Value	P Value	Inferences
RHR	80.85±8.38	81.61±9.60	84.50±8.98	4.828	0.009	Highly Significant
30:15	1.27±0.12	1.32±0.12	1.28±0.12	6.949	0.001	Highly Significant
E: I	1.34±0.08	1.38±0.09	1.35±0.08	5.260	0.006	Highly Significant
Standing: Lying	1.25±0.08	1.26±0.08	1.25±0.10	0.576	0.563	Not Significant
RBP (Systolic)	115.12±6.86	115.49±6.74	116.23±6.49	0.743	0.477	Not Significant
RBP (Diastolic)	68.23±7.32	68.19±7.55	70.67±7.39	3.838	0.023	Significant
Supine: Standing (Systolic)	107.28±5.85	105.52±5.65	105.96±5.59	2.691	0.069	Not Significant
Supine: Standing (Diastolic)	64.67±6.65	65.45±6.19	67.5±7.44	4.909	0.008	Significant
CPT (Systolic)	131.47±7.64	131.60±7.82	131.50±8.08	0.008	0.992	Not Significant
CPT (Diastolic)	84.74±8.33	86.36±7.07	87.39±8.15	3.021	0.050	Significant

Among the parasympathetic parameters, resting heart rate showed significant variation across the menstrual cycle (p = 0.009), with the highest mean value observed during the luteal phase. The 30:15 ratio and Expiration: Inspiration (E:I) ratio also demonstrated significant differences (p = 0.001 and p = 0.006, respectively), with the highest values recorded during the follicular phase. The Standing: Lying ratio did not show significant variation across the three menstrual phases (p = 0.563).

Among the sympathetic parameters, resting systolic blood pressure did not differ significantly across the menstrual cycle. However, resting diastolic blood pressure showed significant variation (p = 0.037), with higher values observed during the luteal phase. Similarly, the systolic blood pressure response during the Supine–Standing test and the Cold Pressor Test did not vary significantly across the menstrual phases. In contrast, the diastolic blood pressure responses during both tests showed significant variation (p = 0.009 and p = 0.050, respectively), with the highest values recorded during the luteal phase.

The Bonferroni post hoc comparisons of significant cardiovascular autonomic function parameters are summarized in **Table 3**.

Table 3: Bonferroni Post Hoc Comparison of Significant Cardiovascular Autonomic Function Parameters

Parameter	Phase Comparison	Mean Difference	*p* Value
Resting Heart Rate (beats/min)	Menstrual vs Follicular	0.76	0.813
	Follicular vs Luteal	2.89	0.053
	Luteal vs Menstrual	3.60	0.010*
30:15 Ratio	Menstrual vs Follicular	0.05	0.001*
	Follicular vs Luteal	0.04	0.023*
	Luteal vs Menstrual	0.02	0.611
Expiration:Inspiration (E:I) Ratio	Menstrual vs Follicular	0.04	0.009*
	Follicular vs Luteal	0.03	0.025*
	Luteal vs Menstrual	0.00	0.932
Standing:Lying Ratio	Menstrual vs Follicular	0.01	0.532
	Follicular vs Luteal	0.01	0.855
	Luteal vs Menstrual	0.01	0.851
Resting Diastolic Blood Pressure (mmHg)	Menstrual vs Follicular	0.08	0.999
	Follicular vs Luteal	2.47	0.043*
	Luteal vs Menstrual	2.43	0.047*
Supine–Standing Diastolic Blood Pressure Response (mmHg)	Menstrual vs Follicular	0.78	0.862
	Follicular vs Luteal	2.05	0.073
	Luteal vs Menstrual	2.83	0.007*
Cold Pressor Test Diastolic Blood Pressure Response (mmHg)	Menstrual vs Follicular	–0.80	0.297
	Follicular vs Luteal	–1.84	0.611
	Luteal vs Menstrual	2.64	0.041*

Values are expressed as mean differences obtained by Bonferroni post hoc analysis.
*Statistically significant ($p < 0.05$).
Abbreviations: E:I = Expiration:Inspiration; MP = Menstrual Phase; FP = Follicular Phase; LP = Luteal Phase.

Post hoc analysis demonstrated a significant increase in resting heart rate during the luteal phase compared with the menstrual phase. Significant differences in the 30:15 ratio and E:I ratio were observed between the menstrual and follicular phases and between the follicular and luteal phases. Resting diastolic blood pressure showed significant differences between the luteal phase and both the menstrual and follicular phases. Significant differences were also observed in the diastolic blood pressure response during the Supine–Standing test and the Cold Pressor Test between the menstrual and luteal phases. No significant pairwise differences were observed for the Standing: Lying ratio.

DISCUSSION

The present study demonstrated significant phase-dependent variations in cardiovascular autonomic function across the menstrual cycle in healthy young women. Parasympathetic activity, assessed by the 30:15 ratio and Expiration: Inspiration (E:I) ratio, was significantly greater during the follicular phase, whereas resting heart rate, resting diastolic blood pressure, and diastolic blood pressure responses during the Supine–Standing test and Cold Pressor Test were significantly higher during the luteal phase. In contrast, the Standing: Lying ratio and systolic blood pressure parameters did not differ significantly among the three phases. These findings indicate enhanced vagal modulation during the follicular phase and relative sympathetic predominance during the luteal phase, reflecting the physiological influence of ovarian hormones on cardiovascular autonomic regulation.[1]

The significantly higher 30:15 ratio and E:I ratio observed during the follicular phase suggest increased parasympathetic activity during this phase of the menstrual cycle. The 30:15 ratio and E:I ratio are established indices of vagal function and provide reliable measures of cardiac parasympathetic activity.[5]

The enhanced vagal activity observed during the follicular phase may be attributed to the rising estrogen levels, which improve endothelial nitric oxide production, facilitate vagal modulation, and reduce sympathetic vasoconstrictor activity.[5]

Similar findings have been reported by Priyadharshini et al., Verma et al., Parlewar and Venkatraman, and Patra et al., all of whom demonstrated greater parasympathetic activity during the follicular phase.[12,13,14,15]

Comparable findings were reported by Srujana and Chandala, who demonstrated significantly greater parasympathetic activity during the follicular phase and relative sympathetic predominance during the luteal phase using objective cardiovascular autonomic function tests, thereby supporting the observations of the present study.[23]

In the present study, the Standing: Lying ratio did not show significant variation, suggesting that postural vagal reflexes may be less influenced by cyclical hormonal changes, a finding comparable with that reported by Leicht et al.[19]

The sympathetic function tests demonstrated significantly higher resting diastolic blood pressure and greater diastolic blood pressure responses during the Supine–Standing test and Cold Pressor Test in the luteal phase, indicating increased sympathetic vasomotor activity. Although resting systolic blood pressure did not differ significantly across the menstrual cycle, the rise in diastolic blood pressure during the luteal phase suggests increased peripheral vascular resistance associated with progesterone predominance.[3] Progesterone has

been shown to influence sympathetic outflow, vascular reactivity, and baroreceptor sensitivity, thereby contributing to the observed autonomic changes.[4] Similarly, Minson et al. demonstrated that menstrual cycle–related hormonal fluctuations influence sympathetic neural activity, baroreflex sensitivity, and vascular transduction, providing further evidence that ovarian hormones modulate cardiovascular autonomic regulation throughout the menstrual cycle.[24] These observations are consistent with the findings of Yazar and Yazıcı, Bai et al., and Matsumoto et al., who reported greater sympathetic activity during the luteal phase.[6,8,9] The present findings also agree with Jasrotia et al., who demonstrated increased cardiovascular reactivity during the luteal phase using the Cold Pressor Test.[22]

Resting heart rate was also significantly higher during the luteal phase. Although heart rate reflects the combined influence of sympathetic and parasympathetic activity, an elevated resting heart rate generally indicates reduced vagal tone together with relative sympathetic predominance.[1] Similar observations have been reported by Rani and Venkatesh, whereas Yildirir et al. demonstrated reduced parasympathetic modulation during the luteal phase using heart rate variability analysis.[21,7] However, some investigators, including Fuenmayor et al. and Chung and Yang, reported differing patterns of autonomic activity during the menstrual cycle.[10,11] These discrepancies among studies may be explained by differences in study populations, sample size, methods used to determine menstrual phase, hormonal status, and the autonomic parameters evaluated. Hirshoren et al. further demonstrated that cyclical changes in estrogen and progesterone are associated with alterations in both neurohumoral and autonomic mechanisms regulating the cardiovascular system, emphasizing the physiological basis for the phase-dependent autonomic variations observed in the present study.[25]

The findings of the present study emphasize the importance of considering the menstrual phase when evaluating cardiovascular autonomic function in women of reproductive age. Physiological hormonal fluctuations may influence autonomic test results and should therefore be considered during both clinical assessment and physiological research. The study was limited by its cross-sectional design, single-center setting, and the absence of direct estimation of serum estrogen and progesterone levels. Nevertheless, the use of multiple standardized cardiovascular autonomic function tests enabled a comprehensive assessment of both sympathetic and parasympathetic function across all three phases of the menstrual cycle.

CONCLUSION

The present study demonstrated significant phase-related variations in cardiovascular autonomic function during the menstrual cycle in healthy young women. Parasympathetic activity, reflected by higher 30:15 and Expiration: Inspiration (E:I) ratios, was significantly enhanced during the follicular phase, whereas resting heart rate, resting diastolic blood pressure, and diastolic responses to the Supine–Standing test and Cold Pressor Test were significantly greater during the luteal phase, indicating relative sympathetic predominance.[1,5] These findings support the physiological role of ovarian hormones in modulating cardiovascular autonomic function and highlight the importance of considering menstrual phase during autonomic assessment in women of reproductive age. The study also provides baseline data for future investigations exploring the relationship between hormonal fluctuations and cardiovascular autonomic regulation.

Future Scope

Further studies involving larger and more diverse populations are required to validate the findings of the present study. Simultaneous estimation of serum estrogen and progesterone levels would provide a better understanding of the relationship between hormonal fluctuations and cardiovascular autonomic function. The inclusion of advanced autonomic assessment techniques, such as heart rate variability analysis, baroreflex sensitivity, and continuous blood pressure monitoring, may further clarify the mechanisms underlying autonomic modulation during the menstrual cycle. Longitudinal multicenter studies may also help establish the clinical significance of these physiological changes in women with cardiovascular or autonomic disorders.

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