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CHANGES IN PARASYMPATHETIC CARDIOVASCULAR AUTONOMIC FUNCTIONS DURING THE MENSTRUAL CYCLE IN MEDICAL STUDENTS FROM BIDAR, KARNATAKA: A DESCRIPTIVE CROSS-SECTIONAL STUDY

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ABSTRACT

The menstrual cycle is associated with cyclical fluctuations in estrogen and progesterone that influence cardiovascular autonomic regulation through modulation of parasympathetic activity. This study evaluated changes in parasympathetic cardiovascular autonomic function across different phases of the menstrual cycle in healthy young female medical students. A cross-sectional observational study was conducted among 105 healthy female medical students aged 18–21 years at Bidar Institute of Medical Sciences, Karnataka. Participants underwent autonomic function testing during the menstrual, follicular, and luteal phases of a single menstrual cycle. Parasympathetic cardiovascular function was assessed using resting heart rate (RHR), the 30:15 ratio, the Expiration: Inspiration (E:I) ratio, and the Standing: Lying (S:L) ratio. Data were analyzed using repeated-measures analysis of variance followed by Bonferroni post-hoc comparisons, with statistical significance set at $p < 0.05$. The 30:15 ratio and E:I ratio were significantly higher during the follicular phase than during the menstrual and luteal phases ($p = 0.001$ and $p = 0.006$, respectively), indicating enhanced parasympathetic activity. Resting heart rate differed significantly across menstrual phases ($p = 0.009$), whereas the Standing:Lying ratio showed no significant variation ($p = 0.563$). These findings demonstrate that parasympathetic cardiovascular autonomic function varies across the menstrual cycle, with greater vagal activity during the estrogen-dominant follicular phase. Consideration of menstrual phase may therefore improve the interpretation of cardiovascular autonomic function tests in healthy young women.

Keywords: Menstrual Cycle, Cardiovascular Autonomic Function, Parasympathetic Nervous System, Resting Heart Rate, 30:15 Ratio, Expiration: Inspiration Ratio.

INTRODUCTION

Menstrual is a Latin word meaning mensis, i.e. lunar month of 28 days^[1], as it was observed to occur once every month. The menstrual cycle is defined by the regular, repetitive monthly occurrence of ovulation throughout a woman's reproductive life and is divided into ovarian and uterine cycle phases. It is more accurately termed the “female monthly sexual cycle”^[2]. Although the length of the cycle is variable among individuals, the average duration is 28 days from the onset of one menstrual period to the next.^[3] Normal reproductive function depends on the precise quantitative and temporal regulation of the hypothalamic-pituitary-ovarian (HPO) axis^[4].

This axis involves three hormonal levels - Gonadotropin-releasing hormone (GnRH) from the hypothalamus, Follicle-stimulating hormone (FSH) and luteinizing hormone (LH) from the anterior pituitary, and Estrogen and progesterone from the ovaries, secreted in response to the pituitary hormones.^[2]

These hormones are secreted at significantly varying rates during the different phases of the menstrual cycle. In the menstrual phase, levels of estrogen and progesterone fall sharply, resulting in endometrial shedding, while FSH begins to rise and LH remains low^[5]. During the follicular phase, the rising FSH promotes follicular development, leading to an increase in estrogen secretion, which in turn stimulates endometrial proliferation; progesterone remains low during this phase^[6]. In the luteal phase, FSH and LH levels decline, estrogen levels stabilize at a moderate level, and progesterone reaches its peak due to corpus luteum activity, preparing the endometrium for potential implantation^[6]. If fertilization does not occur, estrogen and progesterone drop again, restarting the cycle^[1]



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The cardiovascular system is tightly regulated by the autonomic nervous system (ANS), which maintains homeostasis through the coordinated actions of its sympathetic and parasympathetic divisions [7]. Among these, parasympathetic activity—primarily mediated through the vagus nerve—has a cardioprotective role by modulating heart rate variability and maintaining resting heart rate. Fluctuations in ovarian hormones, particularly estrogen, are known to enhance vagal tone, while progesterone tends to attenuate it. [8]

Autonomic Function Tests (AFTs), such as the 30:15 ratio and Expiration:Inspiration (E:I) ratio, offer non-invasive means to evaluate parasympathetic cardiovascular function across menstrual phases. These tests have shown phase-dependent changes, reflecting underlying hormonal influence [9]. However, existing literature on this subject is limited. Several prior studies either focused on postmenopausal populations [10], involved small sample sizes [11][12], or examined only one or two menstrual phases [13], leading to inconclusive and inconsistent findings. There remains a notable gap in understanding how all three phases of the normal menstrual cycle distinctly affect parasympathetic autonomic regulation. Therefore, the present study was undertaken to assess parasympathetic cardiovascular function during the menstrual, follicular, and luteal phases of the cycle. The outcomes of this study may have significant implications in the diagnostic and therapeutic contexts of modern medicine and neurology, especially in understanding sex-specific autonomic regulation.

MATERIALS AND METHODS

Study Design

A cross-sectional observational study was conducted in the Department of Physiology, Bidar Institute of Medical Sciences (BRIMS), Bidar, Karnataka, India, over a period of one year and six months. The study evaluated parasympathetic cardiovascular autonomic function during different phases of the menstrual cycle among healthy young female medical students.

Study Participants

A total of 128 female medical students were screened for eligibility. After applying the inclusion and exclusion criteria, 105 healthy female students aged 18–21 years were enrolled using simple random sampling. Written informed consent was obtained from all participants before enrolment.

Inclusion Criteria

Participants who fulfilled all of the following criteria were included:

- Healthy female medical students aged 18–21 years

- Regular ovulatory menstrual cycles (27–30 days)
- Eumenorrheic
- Unmarried and nulliparous
- Normotensive
- Non-obese
 - Willing to participate in the study

Exclusion Criteria

Participants were excluded if they had:

- Irregular menstrual cycles or suspected anovulatory cycles
- Pregnancy
- Hypertension, diabetes mellitus, thyroid disorders, 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 known to affect hormonal status or autonomic function

Data Collection

Baseline demographic and anthropometric data, including age, height, weight, and body mass index (BMI), were recorded. BMI was calculated using the Quetelet Index.

Each participant underwent autonomic function testing during three phases of a single menstrual cycle:

- Menstrual phase: Days 1–4
- Follicular phase: Days 5–14
- Luteal phase: Days 15–28 or until the onset of the next menstrual period

All recordings were performed between 9:00 a.m. and 11:00 a.m. in a quiet, temperature-controlled laboratory. Participants were instructed to avoid heavy meals, caffeinated beverages, and strenuous physical activity for at least one hour before testing and were allowed to rest for 30 minutes before the recordings.

Assessment of Parasympathetic Cardiovascular Autonomic Function

Parasympathetic cardiovascular autonomic function was evaluated using a digital physiograph (Physio-Pac, Medicaid Systems) by performing the following standardized autonomic function tests:

Resting Heart Rate (Rhr)

Resting heart rate was recorded in the supine position after 10 minutes of rest using Lead II electrocardiography (ECG). Heart rate was calculated from the R-R interval.

Deep Breathing Test (Expiration:Inspiration Ratio)

Participants performed deep breathing at a rate of six breaths per minute. The Expiration:Inspiration (E:I) ratio was calculated using the longest R-R interval during expiration divided by the shortest R-R interval during inspiration.

Heart Rate Response To Standing (30:15 Ratio)

Participants moved rapidly from the supine to the standing position while continuous ECG recording was obtained. The 30:15 ratio was calculated as the ratio of the longest R-R interval around the 30th heartbeat to the shortest R-R interval around the 15th heartbeat after standing.

Standing-To-Lying (S:L) Ratio

The Standing:Lying ratio was determined from ECG recordings obtained while participants changed from the standing to the supine position. The ratio was calculated using standard autonomic function testing procedures.

Statistical Analysis

Data were entered into Microsoft Excel and analyzed using IBM SPSS Statistics version 18.0. Continuous variables were expressed as mean $\pm$ standard deviation (SD). Comparisons of autonomic function parameters across the menstrual, follicular, and luteal phases were performed using repeated-measures analysis of variance (ANOVA). Bonferroni post hoc analysis was used 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 prior to enrolments. Participant confidentiality was maintained throughout the study.

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 (Table 1).

Resting Heart Rate

The mean resting heart rate differed significantly across the three phases of the menstrual cycle ($F = 4.828$, $p = 0.009$). The highest mean resting heart rate was observed during the luteal phase (84.50 ± 8.98 beats/min), while the lowest value was recorded during the menstrual phase (80.85 ± 8.38 beats/min). Bonferroni post hoc analysis demonstrated a significant difference between the luteal and menstrual phases ($p = 0.010$), whereas differences between the menstrual and follicular phases ($p = 0.813$) and between the follicular and luteal phases ($p = 0.053$) were not statistically significant (Tables 2 and 3).

Heart Rate Response To Standing (30:15 Ratio)

The mean 30:15 ratio showed a significant variation across the menstrual cycle ($F = 6.949$, $p = 0.001$). The highest mean value was observed during the follicular phase (1.32 ± 0.12). Post hoc analysis revealed significant differences between the menstrual and follicular phases ($p = 0.001$) and

between the follicular and luteal phases ($p = 0.023$). No significant difference was observed between the luteal and menstrual phases ($p = 0.611$) (Tables 2 and 4).

Expiration:Inspiration (E:I) Ratio

The mean E:I ratio differed significantly among the three menstrual phases ($F = 5.260$, $p = 0.006$). The highest mean value was recorded during the follicular phase (1.38 ± 0.09). Pairwise comparisons demonstrated significant differences between the menstrual and follicular phases ($p = 0.009$) and between the follicular and luteal phases ($p = 0.025$), whereas the difference between the luteal and menstrual phases was not statistically significant ($p = 0.932$) (Tables 2 and 5).

Standing:Lying Ratio

The Standing:Lying ratio did not differ significantly across the menstrual, follicular, and luteal phases ($F = 0.576$, $p = 0.563$). Likewise, pairwise comparisons between menstrual and follicular phases ($p = 0.532$), follicular and luteal phases ($p = 0.855$), and luteal and menstrual phases ($p = 0.851$) showed no statistically significant differences (Tables 2 and 6).

DISCUSSION

The present study evaluated parasympathetic cardiovascular autonomic function across different phases of the menstrual cycle in 105 healthy female medical students using standardized autonomic function tests. Significant variations were observed in resting heart rate (RHR), the 30:15 ratio, and the Expiration:Inspiration (E:I) ratio, whereas the Standing:Lying (S:L) ratio remained unchanged across the menstrual cycle. These findings indicate that parasympathetic cardiovascular regulation varies with hormonal fluctuations occurring during the menstrual cycle.

Resting Heart Rate

Resting heart rate showed significant variation across the menstrual cycle, with the highest values observed during the luteal phase and the lowest during the menstrual phase. Pairwise analysis demonstrated a significant difference only between the luteal and menstrual phases. Similar findings have been reported by Kavitha et al., Shaily et al., and Christina et al., who observed lower resting heart rate during the follicular phase, suggesting greater parasympathetic influence during this phase^{[14][15][16]}. Studies by Parlewar et al., Rajani et al., and Veena et al. also reported no significant difference between the follicular and luteal phases, consistent with the present findings^{[17][18][19]}. Differences among published studies may be explained by variations in study populations, phase determination, hormonal status, and methodological differences.

Heart Rate Response To Standing (30:15 Ratio)

The 30:15 ratio demonstrated significant variation across menstrual phases, with the highest values during the follicular phase. Significant differences were observed between the menstrual and follicular phases and between the follicular and luteal phases. These findings are consistent with studies by Shikha et al., Karthika et al., Shaily et al., and Subhadeep et al., all of whom reported greater parasympathetic activity during the follicular phase^{[20][21][15][13]}. Estrogen has been shown to enhance vagal activity through increased nitric oxide production, modulation of muscarinic receptors, and suppression of sympathetic neurotransmission, whereas progesterone exerts the opposite effect during the luteal phase.

Expiration:Inspiration Ratio

The E:I ratio also showed significant phase-related variation, with the highest values during the follicular phase. These observations are comparable with those reported by Shikha et al., Kavitha et al., Shaily et al., and Subhadeep et al., who demonstrated enhanced cardiovagal modulation during the estrogen-dominant follicular phase^{[20][14][15][13]}. Although Parlewar et al. and Christina et al. reported less pronounced differences, the overall evidence supports the influence of ovarian hormones on parasympathetic cardiovascular control^{[17][16]}.

Standing:Lying Ratio

Unlike the other autonomic function tests, the Standing:Lying ratio did not show statistically significant variation across the menstrual cycle. Similar observations have been reported by Veena et al. and Parlewar et al., suggesting that postural cardiovascular reflexes remain relatively stable despite hormonal fluctuations^{[19][17]}. This may reflect preservation of homeostatic autonomic reflexes that are less susceptible to cyclical hormonal modulation than other indices of vagal activity.

Physiological Significance

The observed increase in parasympathetic activity during the follicular phase is consistent with the physiological actions of estrogen, which enhances vagal tone through central and peripheral autonomic mechanisms. In contrast, the progesterone-dominant luteal phase is associated with reduced parasympathetic modulation and relatively greater sympathetic influence. These hormonal effects likely explain the cyclical variation observed in autonomic cardiovascular function.

Strengths And Limitations

The present study assessed all three phases of a complete menstrual cycle using standardized autonomic function tests in a relatively homogeneous population of healthy young women. However, some limitations should be acknowledged. The study included participants from a single institution, limiting the generalizability of the

findings. Hormonal assays were not performed to confirm menstrual phase, and autonomic assessment was limited to parasympathetic function tests without heart rate variability analysis.

CONCLUSION

The present study demonstrates that parasympathetic cardiovascular autonomic function varies significantly across different phases of the menstrual cycle in healthy young female medical students. The significantly higher 30:15 ratio and Expiration:Inspiration ratio during the follicular phase indicate enhanced parasympathetic activity, while the higher resting heart rate observed during the luteal phase suggests reduced vagal modulation. In contrast, the Standing:Lying ratio remained unchanged throughout the menstrual cycle.

These findings support the concept that cyclical fluctuations in estrogen and progesterone influence cardiovascular autonomic regulation. Recognition of these physiological variations is important when interpreting autonomic function tests in women of reproductive age and may help improve the clinical evaluation of cardiovascular and autonomic disorders. Further studies involving larger and more diverse populations, with hormonal assays and additional autonomic function measures such as heart rate variability, are warranted to better understand the clinical implications of menstrual cycle-related autonomic changes.

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Conflict of interest

The authors declare no conflicts of interest regarding this study.

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Tables and Graphs

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
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Table 2: Mean and Standard Deviation (SD) of Parasympathetic Parameters in All 105 Subjects (N=105)

Aft Parameters	Mp	Fp	Lp	F Value	P Value
	Mean ± Sd	Mean ± Sd	Mean ± Sd		
Rhr	80.85±8.38	81.61±9.60	84.50±8.98	4.828	0.009
30:15	1.27±0.12	1.32±0.12	1.28±0.12	6.949	0.001
E: I	1.34±0.08	1.38±0.09	1.35±0.08	5.260	0.006
Standing: Lying	1.25±0.08	1.26±0.08	1.25±0.10	0.576	0.563

Table 3: Table Showing the Comparison of Difference in Mean of RHR

Phases	Difference In Mean	P Value
MP Vs FP	0.76	0.813
FP Vs LP	2.89	0.053
LP Vs MP	3.6	0.010

Table 4: Table Showing the Comparison of Mean Difference of 30:15

Phases	Mean Difference	P Value
MP Vs FP	0.057	0.001
FP Vs LP	0.042	0.023
LP Vs MP	0.015	0.611

Table 5: Table Showing the Comparison of Difference of E: I

Phases	Mean Difference	P Value
MP Vs FP	0.034	0.009
FP Vs LP	0.03	0.025
LP Vs MP	0.004	0.932

Table 6: Table Showing the Comparison of Mean Difference of Standing: Lying

Phases	Mean Difference	P Value
MP Vs FP	0.013	0.532
FP Vs LP	0.006	0.855
LP Vs MP	0.006	0.851