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Original Research Article

Assessment of cardiac autonomic functions and anxiety sensitivity scale in different phases of menstrual cycle in young females

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ABSTRACT

Background: The menstrual cycle, a reproductive rhythm marked by bleeding and ovulation, is a dynamic biological process where hormones quietly reshape multiple systems in the body with their fluctuations. Cardiovascular control, emotional reactivity and stress responsiveness are the changes which become relevant in young women. Objectives were to measure heart rate variability (HRV) and anxiety sensitivity in different phases of menstrual cycle and establish their correlation.
Methods: This study was a comparative (observational) consisting of 48 healthy females' participants aged 18-32 years. Cardiac autonomic function was assessed using HRV analysis on day 2, day 10, and day 21 of the menstrual cycle While anxiety sensitivity was assessed using the anxiety sensitivity index-3 (ASI-3), an 18-item scale, containing items specifying different concerns someone could have regarding their anxiety. The total ASI-3 score was analysed and compared across the menstrual phases to observe variations in anxiety sensitivity. Correlation between HRV parameters and anxiety sensitivity scores was also assessed to study the relationship between cardiac autonomic function and anxiety sensitive.
Results: Both time-domain and frequency-domain HRV parameters, remained largely stable across follicular, and luteal phases. No statistically significant phase-wise differences were observed. In contrast, anxiety sensitivity exhibited a statistically significant variation across menstrual cycle phases, reflecting meaningful phase-related psychological fluctuation. However, this variation in anxiety sensitivity was not accompanied by corresponding changes in resting HRV parameters, and no consistent association was identified between anxiety sensitivity categories and cardiac autonomic indices across phases.

Keywords: Autonomic nervous system, Heart rate variability, Anxiety sensitivity index-3, Body mass index

INTRODUCTION

The menstrual cycle, a reproductive rhythm marked by bleeding and ovulation, is a dynamic biological process where hormones quietly reshape multiple systems in the body with their fluctuations. Cardiovascular control, emotional reactivity, and stress responsiveness are the changes which become relevant in young women.[1] Cardiac autonomic regulation, most sensitive to hormonal variation, is the balance between autonomic activities which determines variable heart rate behaviour, adjusting the cardiovascular system to rest, stress, and environmental changes. Heart rate variability (HRV), non-invasive marker to record this balance, reflects the tuning of cardiac rhythm by autonomic inputs, especially useful for studying physiological changes that are practical rather than pathological.[2] In women, this autonomic modulation does not stay the same during the whole month. Studies has shown that autonomic control of the heart varies throughout the menstrual phases. Estrogen-dominating

phases relatively enhance parasympathetic activities, in other hand progesterone-dominant phases mostly show an inclination toward sympathetic supremacy. Numerically, these variations seem minor but they demonstrate significant shift in cardiovascular adaptability and stress handling.[3] Such outcomes show that depending on the phase, menstrual cycle, itself can be a cause of nervous strain, exquisitely impacting autonomic responsiveness even in daily, non-stressful conditions. Physiological changes, emotional and cognitive, fluctuate during the menstrual cycle such as mood swings, cognitive load, and emotional changes at different times of the month, even in healthy women with no clinical disorder. studies have shown that anxiety-related experiences and stress perception can differ throughout the menstrual phases. It shows that hormonal transformations extend beyond the heart to brain circuits involved in emotional regulation.[4]

Importantly, these changes are not same in all individuals, reflecting that underlying sensitivity to internal bodily sensations, may play a role. Anxiety sensitivity such as palpitations, breathlessness or dizziness, is a construct capture which shows individuals response towards sensations related to anxiety, especially relevant when studying physiological systems like cardiac autonomic function, where bodily sensations are continuously generated and perceived.[5] There is also a practical need from a research and clinical perspective. Establishing normal phase-related variations in cardiac autonomic function and anxiety sensitivity in healthy females helps create a physiological reference framework. Studying these parameters in apparently healthy women ensures that observed changes reflect normal regulatory patterns rather than disease-driven alterations.

This study rested on the understanding that the menstrual cycle represents a naturally occurring model of hormonal fluctuation in healthy women. Thus, the study was designed to offer clarity at the intersection of autonomic regulation and anxiety sensitivity within the natural rhythm of the menstrual cycle.

METHODS

This study was a comparative (observational) conducted in the Department of Physiology at King George's Medical University, Lucknow, over a period of one year since September 2024 to March 2025. Recruitment was carried out on voluntary 48 healthy participants after taking a detailed medical and menstrual history and applying the predefined inclusion criteria such as females of age 18-32 year of regular cycle, non-alcoholic, non-smoker, non-tobacco, not on any medicines and excluded PCOD, lactating and of irregular menstrual cycle or with any disease. Ethical approval and written informed consent were obtained from the institution and from all subjects respectively. Sample size was calculated on the basis of variation in least significant parameter of HRV in Menstrual and Proliferative phases with 95% confidence level and 90% study power. A total of 48 participants were enrolled and firstly baseline parameters of all subjects were recorded such as age and gender. Later on, body mass index (BMI) was calculated along with detailed menstrual history. Cardiac autonomic function was assessed using HRV analysis on day 2, day 10, and day 21 of the menstrual cycle. Testing was performed in the ANS laboratory of the Department of Physiology, KGMU, Lucknow, using KODYSCAN software. Prior to testing, subjects had to avoided tea, coffee, and any medication; lie comfortably in the supine position. Thereafter electrodes were placed using conduction jelly on the right arm, left arm, and left leg. HRV was recorded for a duration of 5 minutes. While anxiety sensitivity was assessed using the ASI-3, an 18-item scale, containing items specifying different concerns someone could have regarding their anxiety.

For the analysis of cardiac autonomic function, HRV parameters were assessed at different phases of the menstrual cycle to evaluate autonomic nervous system activity. Time-domain and frequency-domain HRV parameters were analysed to study sympathovagal modulation. These parameters were compared across the selected menstrual phases to identify phase-related variations in cardiac autonomic regulation. On the other hand, for the anxiety sensitivity, the ASI-3 scores were used to assess anxiety-related concerns during different phases of the menstrual cycle.

The total ASI-3 score was analysed and compared across the menstrual phases to observe variations in anxiety sensitivity. Correlation between HRV parameters and anxiety sensitivity scores was also assessed to study the relationship between cardiac autonomic function and anxiety sensitivity.

Finally, data were entered in Microsoft excel 2016 and analysed using SPSS version 23. A p value of less than 0.05 was considered statistically significant.

RESULTS

The study included 48 female participants with a mean age of 20.90±2.41 years, ranging from 18 to 32 years. The mean body weight of the participants was 55.79±6.61 kg, with values ranging between 40 and 75 kg. The mean height was recorded as 158.77±5.28 cm, with a minimum of 149 cm and a maximum of 172 cm. The mean BMI of the participants was 22.34±3.09 kg/m², and BMI values ranged from 16.57 to 30.82 kg/m². The baseline demographic and anthropometric characteristics of the study participants were summarised in Table 1.

Ordinal analysis of anxiety sensitivity across the menstrual cycle phases was presented in Table 4. Friedman test demonstrated a statistically significant difference in anxiety sensitivity scores across the three phases of the menstrual cycle, with a chi-square value of 8.91 and a corresponding p=0.012.

Table 1: Baseline demographic and anthropometric characteristics of the study participants, (n=48).

Characteristics	Mean±SD	Range (minimum-maximum)
Age (in years)	20.90±2.41	18-32
Weight (kg)	55.79±6.61	40-75
Height (cm)	158.77±5.28	149-172
BMI (kg/m²)	22.34±3.09	16.57-30.82

Table 2: HRV-time domain parameters across menstrual cycle phases.

Parameters	Day 2 (Menstrual)	Day 10 (Follicular)	Day 21 (Luteal)	Test	P value
SDNN (ms)	48.79±20.04	50.29±17.55	49.55±25.95	RM-ANOVA	0.888
RMSSD (ms)	56.27±32.41	53.09±25.12	56.18±40.50	RM-ANOVA	0.803
NN50 (count)	87.75±72.72	76.10±56.72	80.88±69.99	Friedman test	0.447
pNN50 (%)	25.11±23.69	21.14±17.63	23.06±22.41	Friedman test	0.532

Table 3: HRV-frequency domain parameters across menstrual cycle phases.

Parameters	Day 2 (Menstrual)	Day 10 (Follicular)	Day 21 (Luteal)	Test	P value
Total power (ms²)	2716.76±2181.91	3202.24±6652.03	2838.97±3816.90	Friedman test	0.726
LF power (ms²)	762.69±650.86	1166.51±3361.93	776.11±840.67	Friedman test	0.495
HF power (ms²)	1345.11±1987.47	1299.48±1913.06	1439.47±3019.12	Friedman test	0.949
LF norm (nu)	47.53±20.35	50.76±22.52	47.26±24.32	RM-ANOVA	0.505
HF norm (nu)	52.46±20.35	49.23±22.52	52.73±24.32	RM-ANOVA	0.505
LF/HF ratio	1.28±1.17	1.47±1.66	1.52±1.77	Friedman test	0.641

Table 4: Distribution of ASI categories across menstrual cycle phases.

Parameters	Test	χ^2 value	P value
Anxiety sensitivity (ASI score)	Friedman test	8.91	0.012

Table 5: Statistical comparison of HRV parameters across menstrual cycle phases.

Parameters	F value/χ^2	P value	Statistical test
Pulse rate	0.98	0.380	Repeated measures ANOVA
Mean R-R	1.25	0.291	Repeated measures ANOVA
SDNN	0.12	0.888	Repeated measures ANOVA
RMSSD	0.22	0.803	Repeated measures ANOVA
LF/HF ratio	0.89	0.641	Friedman test

Table 6: Non-parametric association between HRV and anxiety category by phase.

Phases	HRV parameter	Anxiety category comparison	P value
Day 21	RMSSD (ms)	Low vs moderate	0.482
Day 21	LF/HF Ratio	Low vs moderate	0.537
Day 10	SDNN (ms)	Low vs moderate	0.623

*Mann-Whitney U

Table 7: HRV in subgroups by dominant anxiety pattern.

Subgroups	N	SDNN day 21 (ms)	RMSSD day 21 (ms)	LF/HF ratio day 21
Consistent low ASI	15	52.14±28.73	62.41±45.29	1.23±1.15
Variable ASI pattern	25	48.72±25.11	53.88±39.67	1.69±2.07
Consistent moderate ASI	8	46.88±24.55	50.63±37.82	1.59±1.45

The statistical comparison of HRV parameters across different phases of the menstrual cycle was summarised in Figure 1. Repeated measures ANOVA showed no statistically significant difference in pulse rate across the menstrual cycle phases, with an F=0.98 and a p=0.380. Similarly, mean R-R interval did not demonstrate a

significant phase-wise difference, with an F=1.25 and a p=0.291.

Time-domain HRV parameters, including SDNN and RMSSD, also did not show statistically significant variation across the menstrual cycle phases. The F value for SDNN was 0.12 with a p=0.888, while RMSSD showed an F=0.22 and a p=0.803, indicating no significant differences across phases. The LF/HF ratio, analysed using the Friedman test, also did not demonstrate a statistically significant difference across the menstrual cycle phases, with a chi-square value of 0.89 and a p=0.641.

The transition of anxiety sensitivity categories across the menstrual cycle phases was presented in Figure 2. Out of 48 participants, 15 (31.25%) maintained a consistently low anxiety sensitivity category across all three phases of the menstrual cycle. A total of 25 participants (52.08%) demonstrated a variable pattern, with changes in anxiety sensitivity category between phases. Additionally, 8 participants (16.67%) consistently remained in the moderate anxiety sensitivity category across all phases.

Non-parametric comparisons between HRV parameters and anxiety sensitivity categories were presented in Figure 3. On day 21 of the menstrual cycle, RMSSD values did not differ significantly between participants with low and moderate anxiety sensitivity, with a p=0.482. Similarly, the LF/HF ratio on day 21 showed no statistically significant difference between the low and moderate anxiety categories (p=0.537). On day 10 of the menstrual cycle, comparison of SDNN values between low and moderate anxiety sensitivity categories also did not demonstrate a statistically significant difference, with a p=0.623, as shown in Figure 3.

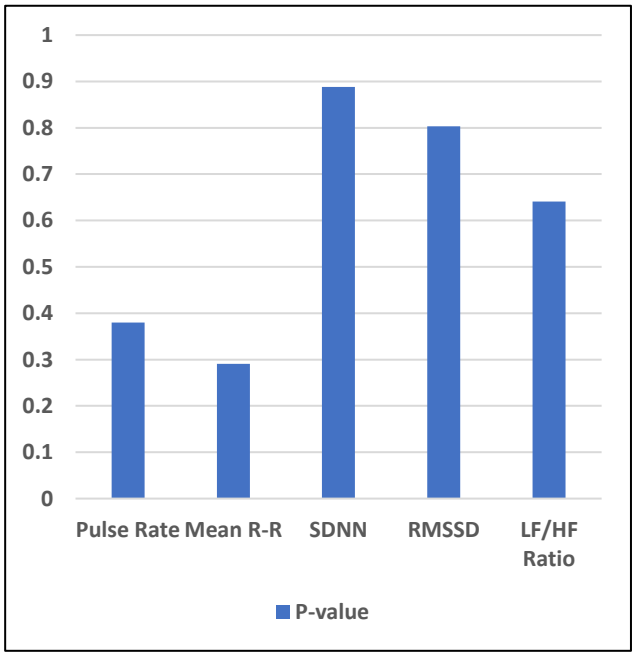

Figure 1: Statistical comparison of HRV parameters across menstrual cycle phases.

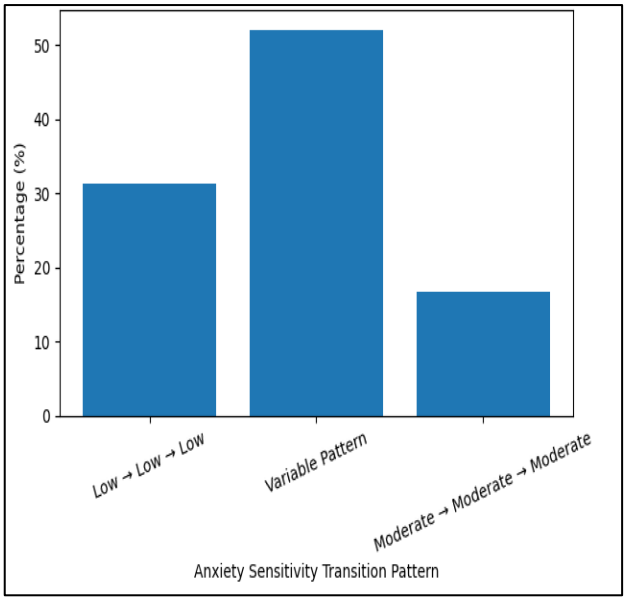

Figure 2: Transition of anxiety sensitivity categories across menstrual cycle phases.

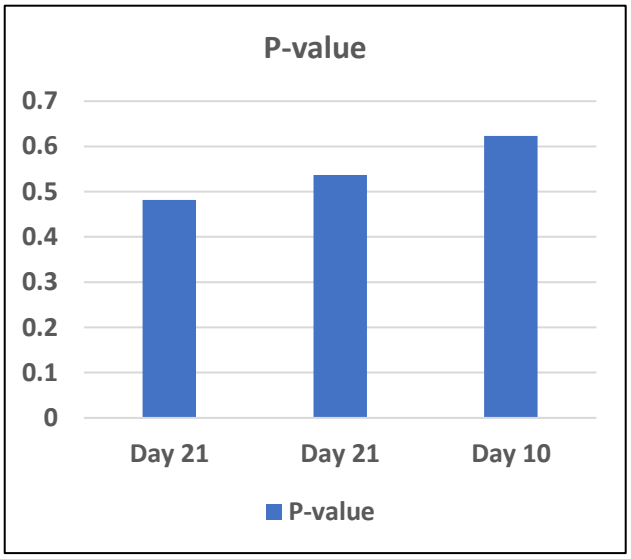

Figure 3: Non-parametric association between HRV and anxiety category by phase.

DISCUSSION

Anxiety is outcome of serotonin alteration, decrease in GABA, enhanced HPA axis which increases cortisol and decrease in brain derived neurotrophic factors. Phasic Menstrual cycle modulates to high estrogen in follicular phase which relax mood by increasing serotonin and decreasing cortisol. While high luteal phase progesterone metabolizes to allopregnanolone which acts as strong anxiolytic as well as sedative. Paradoxically rapid fluctuation in pre-menstrual phase reduced sensitivity to allopregnanolone causes irritability and mood swing. Progesterone as mild CNS depressant produces dysphoria. Anxiety is result of altercation in sensitivity of GABA and MAO receptors mainly.

The study included 48 apparently healthy females with a mean age of 20.90±2.41 years (range: 18-32 years). The mean body weight was 55.79±6.61 kg and the mean height was 158.77±5.28 cm. The mean BMI was 22.34±3.09 kg/m². This baseline uniformity was important, as also highlighted in normative HRV studies by Yeragani et al, Leicht et al, Voss et al and Nunan et al.[5-8]

The mean SDNN values during the menstrual phase (Day 2), during the follicular phase (Day 10), and during the luteal phase (Day 21), were with no statistically significant difference across phases (p=0.888). Similarly, RMSSD values showed minimal variation, measuring on day 2, on day 10, and on day 21 (p=0.803). Other parasympathetic-linked indices, including NN50 and pNN50, also did not demonstrate significant phase-wise variation. These findings indicated that short-term vagal modulation and overall beat-to-beat variability remained relatively stable across menstrual cycle phases at the group level. Similar results were reported by Brar et al, Leicht et al, Tenan et al and Schmalenberger et al.[1,2,9,10]

Total power values showed wide inter-individual dispersion but no statistically significant phase-wise variation, with mean values during the menstrual phase (Day 2), during the follicular phase (Day 10), and during the luteal phase (Day 21) (p=0.726). Similarly, low-frequency (LF) power values and high-frequency (HF) power values were of no statistically significant.

The absence of significant variation in both LF and HF normalized units (p=0.505) suggested that sympathovagal balance remained relatively stable across the menstrual cycle in the resting state. In addition, the LF/HF ratio did not show significant phase-wise differences for day 2, day 10, and day 21 respectively (p=0.641).

Similar observations of minimal or absent phase-related differences in frequency-domain HRV parameters among healthy young women had been reported by Leicht et al, Tenan et al and Yildirir et al.[2,9,11]

The mean pulse rate during the menstrual phase (Day 2) was comparable during the follicular phase (Day 10:) and showed a slight increase during the luteal phase (Day 21). However, this variation were not significant on repeated measures analysis (p=0.380), indicate stable HR.

Similarly, the mean R-R interval values demonstrated reduction on day 2 to on day 10 and on day 21, but these differences were not statistically significant (p=0.291). The absence of significant phase-wise variation in both pulse rate and mean R-R interval suggested that the basal cardiac rhythm and overall autonomic set-point were preserved.

Comparable findings of stable resting heart rate and limited phase-related changes in cardiac timing indices across the menstrual cycle have been reported in healthy young women, supporting the view that resting cardiovascular parameters may be relatively insensitive to cyclical hormonal fluctuations in the absence of external stressors or exercise challenges, as observed by Leicht et al, Tenan et al, Yildirir et al and Yazıcı.[2,9,11,12]

Friedman test demonstrated a statistically significant variation in anxiety sensitivity scores by chi-square value of 8.91 and a corresponding p=0.012. This finding indicated that anxiety sensitivity was not uniform across phases and showed meaningful phase-related fluctuation, in contrast to the largely stable autonomic parameters observed.

Of the 48 participants, 15 remained in the low anxiety sensitivity category across all phases, while 8 participants remained in the moderate category. Notably, more than half of the participants demonstrated a variable pattern across different phases. This high proportion of within-individual variability suggested that menstrual cycle-related psychological changes were dynamic. Previous studies examining mood and anxiety-related changes across the menstrual cycle have similarly reported phase-dependent fluctuation in affective and cognitive domains, even when physiological parameters remained relatively stable, supporting the present observations, as reported by Reed et al, Collins et al, Derntl et al and Poromaa et al.[4,13-15]

On day 21 (luteal phase), comparison of RMSSD values between participants with low and moderate anxiety sensitivity did not demonstrate a statistically significant difference (p=0.482). Similarly, the LF/HF ratio on day 21 did not differ significantly between anxiety sensitivity categories (p=0.537). On day 10 (follicular phase), SDNN values also did not show a significant difference between low and moderate anxiety sensitivity groups (p=0.623), indicating the absence of a strong categorical association between resting cardiac autonomic indices and anxiety sensitivity levels.

Participants with a consistently low anxiety sensitivity pattern demonstrated a mean SDNN of 52.14±28.73 ms and a mean RMSSD of 62.41±45.29 ms, whereas those with a variable anxiety sensitivity pattern showed mean SDNN and RMSSD values of 48.72±25.11 ms and 53.88±39.67 ms respectively. Participants with consistently moderate anxiety sensitivity exhibited slightly lower mean SDNN (46.88±24.55 ms) and RMSSD (50.63±37.82 ms) values. Although these trends suggested numerically lower parasympathetic indices with higher or variable anxiety sensitivity, the overlaps in variability indicated that these differences were not robust enough to achieve statistical significance.

Among participants with low anxiety sensitivity, 18 exhibited high RMSSD values (>50 ms) while 14 showed low RMSSD values (≤50 ms). In contrast, participants with moderate anxiety sensitivity were almost evenly distributed between high (n=4) and low (n=5) RMSSD categories. This distribution highlighted considerable

individual variability and suggested that anxiety sensitivity did not uniformly translate into reduced cardiac vagal modulation at rest.

Similar dissociation between anxiety-related traits and resting HRV measures has been reported in previous psychophysiological studies, suggesting that autonomic-anxiety coupling may become more apparent under stress or challenge conditions rather than during baseline recordings, as noted by Schmidt et al and Yeragani et al.[16,17]

Strengths

Assessment of both cardiac autonomic function and anxiety sensitivity provided an integrated physiological–psychological evaluation. Use of standardised short-term HRV recording under controlled laboratory was done and anxiety sensitivity was assessed using a validated instrument (ASI-3). Homogenous population with normal mean BMI (22.34±3.09 kg/m²) minimised confounding due to obesity or chronic illness. Multiple phases (Day 2, say 10 and day 21) were evaluated, enabling phase-wise comparison.

Limitations

Hormonal levels (estrogen and progesterone) were not biochemically measured for different menstrual phases. HRV was assessed only under resting conditions; autonomic responses to stress or exercise were not evaluated. Sample size was modest and limited to young, apparently healthy females, restricting generalisability. Anxiety sensitivity was assessed using self-report measures, which may be influenced by transient emotional states. Single-cycle assessment did not account for inter-cycle variability.

CONCLUSION

Taken together, these findings suggested that menstrual cycle-related influences were more evident in psychological domains than in resting cardiac autonomic function. The results underscored a dissociation between central psychological modulation and peripheral autonomic output under resting conditions, indicating that phase-related changes in anxiety sensitivity did not necessarily signify altered cardiac autonomic control in healthy young women. The hypothesis was partially accepted. Anxiety sensitivity showed a statistically significant variation across different phases of the menstrual cycle ($p=0.012$), supporting the psychological component of the hypothesis. So, by measuring HRV and anxiety sensitivity in females we can provide an important insight into how hormonal changes during the menstrual cycle may influence both cardiovascular regulation and emotional responses. Hormonal fluctuations across different phases of the cycle can affect the balance of the autonomic nervous system and may also contribute to variations in anxiety levels. Overall, understanding these physiological and psychological variations can contribute to better awareness, early identification of autonomic imbalance, and improved management of cardiovascular and psychological well-being in women.

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