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Physiology

A Comparative Study of Sympathetic Function Tests during Different Phases of Menstrual Cycle in Young Healthy Females

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Original Research Article

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Abstract: Autonomic nerve function status may be changed during different phases of menstrual cycle due to fluctuations of serum gonadal hormones level. This alteration in autonomic nerve functions may affect cardiovagal control. To study the variation of Sympathetic function tests during different Phases of menstrual cycle in young healthy females. The present study was carried out on 50 healthy female subjects with normal menstrual cycles between the ages of 18 to 25 years. Various non-invasive Sympathetic function tests during different phases of menstrual cycle were performed that include isometric handgrip exercise test and postural challenge test including resting blood pressure. The results were analysed using ANOVA and student's paired-t test. During the menstrual cycle, we found that there is a significant increase in the resting systolic and diastolic blood pressure in the luteal phase as compared to menstrual and follicular phase. The statistically significant differences in the blood pressure parameters like blood pressure response to isometric handgrip test and postural variation in blood pressure were found between all the phases, with higher values towards the luteal phase. The study concludes that sympathetic activity is highest during luteal phase and lowest in the follicular phase as compared to menstrual phase. This higher sympathetic activity may be correlated with higher estrogen and progesterone levels during the luteal phase of menstrual cycle.
Keywords: Sympathetic function tests, Menstrual cycle, blood pressure.

INTRODUCTION

Rhythmic activities are abundant in biologic systems and the impact of these rhythms on humans is widely recognized. One such rhythm is the human menstrual cycle [1].

The menstrual cycle apart from being a cycle of monthly periods involving endometrial and cervical changes, also is associated with many physical, psychological and behavioural changes. It is neurohormonal cycle controlled by hypothalamo-pituitary-ovarian axis [2].

The menstrual cycle is governed by well coordinated variations in the levels of ovarian estrogen and progesterone which also produces varying responses in different tissues and organs[3].

During a woman's reproductive years, premenstrual symptoms can significantly disrupt her quality of life or can cause physical, psychological and behavioural changes. The disturbing symptoms of Premenstrual Syndrome (PMS) occur during the luteal (premenstrual) phase of ovulatory cycles and disappear shortly after the onset of menstruation[4].

Some studies have reported that there are certain autonomic changes during the menstrual cycle. The varying levels of ovarian hormones in the normal menstrual cycle may be responsible for such changes in autonomic functions. This altered functioning of autonomic nervous system in late luteal phase may be responsible for PMS [5, 6].

Thus, the aim of the study is to find out the effect of autonomic functions on premenstrual stress by performing various autonomic sympathetic function tests in 3 different phases of menstrual cycle.

MATERIALS & METHODS

The present cross-sectional study was carried out in the Department of Physiology, M.G.M. Medical College, Indore (M.P.).

A total of 50 young healthy female medical students with normal menstrual cycle in the age group of 18-25 years were selected for study.

A brief explanation to subjects regarding the procedure was given and written informed consent was taken. The ethical clearance was obtained from the institutional ethical committee.

Only those participants were taken into study that fulfilled our inclusion criteria's.

Inclusion criteria's

Female subjects of 18-25 yr age group, giving consent for test participation in the study

Exclusion criteria's

- Subjects not giving consent for test participation.
- History of alcohol intake.
- History of smoking, tobacco consumption.
- History of hypertension or any other clinical signs of cardiovascular diseases.
- Females with irregular menstrual cycle.
- Subjects receiving drugs known to affect autonomic function, eg: Adrenergic drugs, Adrenergic blocking drugs, Cholinergic agents, Diuretics, Antihypertensive drugs etc.

A thorough history with special attention to the menstrual history was taken. Subjects were instructed to visit the department during each phase of menstrual cycle. 1-5th day, 9-12th day and 19-25th day were selected to represent the menstrual, follicular and luteal phases respectively. Physical parameters like age in years, height in cms and weight in kgs were noted. Electrocardiogram recordings were carried out in Lead II. All tests were carried out in the morning.

The following Sympathetic function tests were performed

Resting Blood Pressure

The subject was asked to lie down comfortably and take rest for 10 min. Then resting blood pressure was measured by auscultatory method with the help of mercury sphygmomanometer.

Postural change in Blood Pressure

The subject was asked to relax completely for a minimum of 10 min. then the subject was asked to stand up and immediately the change in BP was noted. BP was recorded serially for 1-3 min after standing.

Blood Pressure response to Sustained Handgrip

The subject was asked to sit comfortably in chair. Initially the subject was asked to exert maximal strength on hand grip dynamometer with dominant hand. First the maximum voluntary contraction (MVC) was determined and then the subject was asked to exert 30% of MVC for 5 minutes with dominant hand. Diastolic blood pressure was measured in non-dominant hand at rest and at 1 minute interval during handgrip. The maximum rise of blood pressure during 30% of MVC over the resting blood pressure was noted.

STATISTICAL ANALYSIS

In the present study, results were expressed as Mean ± SD. All statistical analysis was done by using SPSS software version 20, ANOVA test, student's paired-t test. ANOVA test used to find out significant variation across the different phases and student's paired-t tests were carried out to study significance of variations between different phases of menstrual cycle. P Value < 0.05 is taken as significant.

Table-1: Mean ± SD of the Anthropometric Parameters

Variables	Mean ± SD
Age (yrs)	19.32 ± 1.150
BMI (kg/m^2)	20.33 ± 2.993

RESULTS

This study was carried out in the Department of Physiology, M.G.M. Medical College & M.Y. Hospital, Indore (M.P.). A total of 50 female medical students without any co-morbidity, in the age group of 18-25 years were studied for a group of sympathetic function tests and the following observations were drawn from the study.

Table-2: Comparison of Sympathetic function tests during different phases of Menstrual cycle

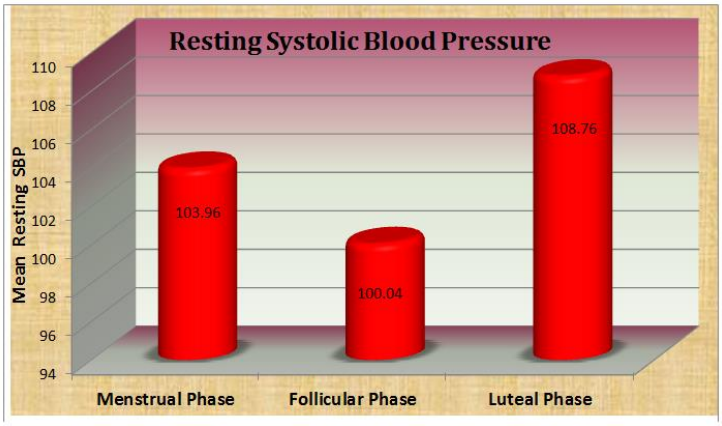
Parameters	Menstrual Phase	Follicular Phase	Luteal Phase	P-value*
Resting SBP	103.96±6.32	100.04±6.03	108.76±6.65	0.000
Resting DBP	69.04±5.20	68.32±4.74	72.08±4.65	0.000
Postural SBP	96.78±5.53	94.24±5.08	99.86±6.16	0.000
Postural DBP	62.76±3.62	62.48±2.97	63.00±3.97	0.345
Sustained handgrip SBP	119.98±6.04	116.22±5.66	126.18±5.92	0.000
Sustained handgrip DBP	87.04±4.90	85.30±4.63	91.20±4.39	0.000

*by ANOVA

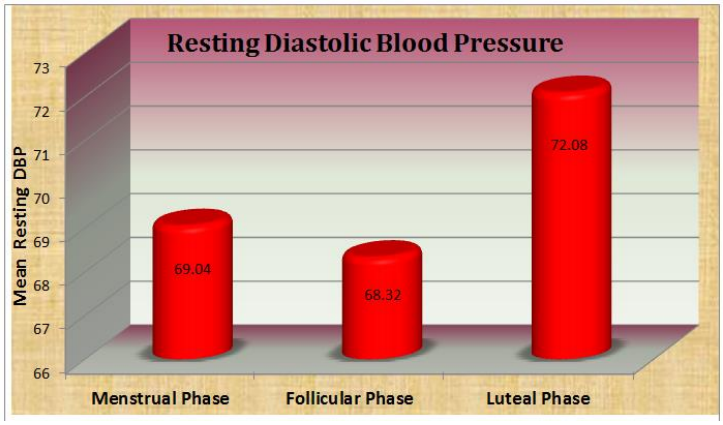
The mean of anthropometric parameters of subjects were described in Table no. 1. The mean ± SD of age in females was 19.32 ± 1.150 yrs and the mean ± SD of BMI in females was 20.33 ± 2.993 kg/m^2.

The mean of all the parameters of sympathetic function tests during different phases of menstrual cycle were described in Table no. 2 and it shows an increase of blood pressure towards the luteal phase, suggestive of sympathetic dominance.

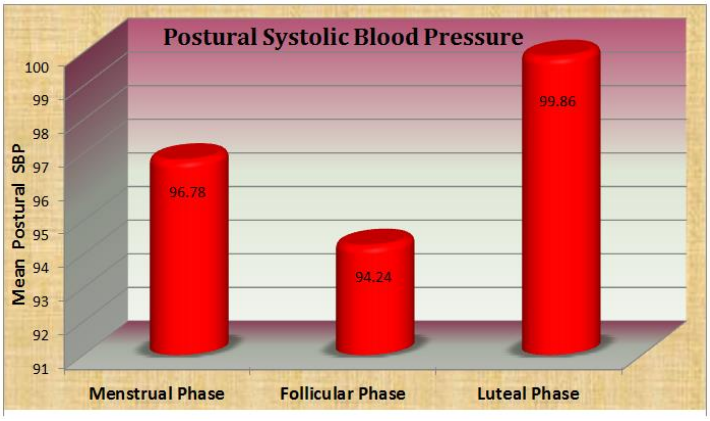
The data obtained was statistically analysed by repeated measures of ANOVA test which shows that there is statistically significant difference in most of the parameters of sympathetic function tests during different phases of menstrual cycle in females.



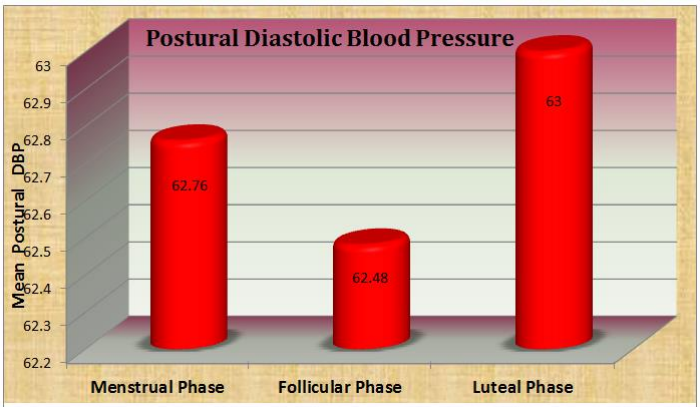
Graph-1: Comparison of Mean Resting Systolic Blood Pressure during different phases of menstrual cycle



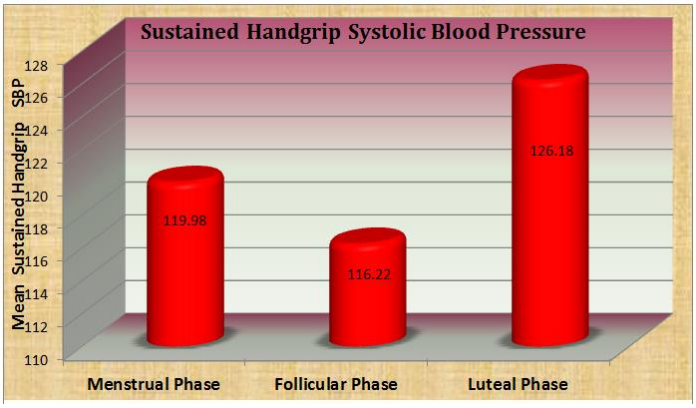
Graph-2: Comparison of Mean Resting Diastolic Blood Pressure during different phases of menstrual cycle



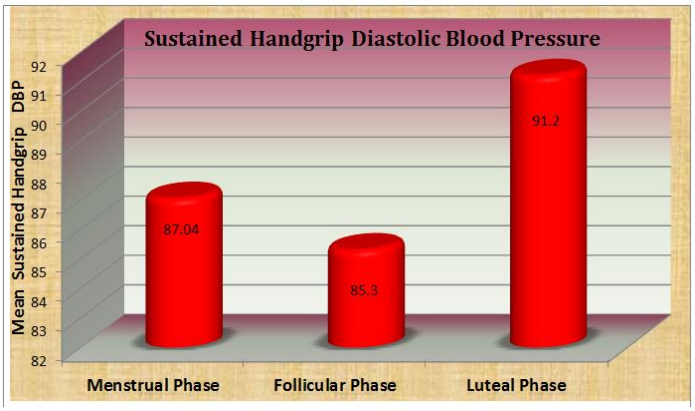
Graph-3: Comparison of Mean Postural Systolic Blood Pressure during different phases of menstrual cycle



Graph-4: Comparison of Mean Postural Diastolic Blood Pressure during different phases of menstrual cycle



Graph-5: Comparison of Mean Sustained Handgrip Systolic Blood Pressure during different phases of menstrual cycle



Graph-6: Comparison of Mean Sustained Handgrip Diastolic Blood Pressure during different phases of menstrual cycle

Table-3: Comparison of Sympathetic function tests between different phases of Menstrual cycle (P-value)*

Parameters	Menstrual Phase v/s Follicular Phase	Menstrual Phase v/s Luteal phase	Follicular Phase v/s Luteal phase
Resting SBP	0.000	0.000	0.000
Resting DBP	0.073	0.000	0.000
Postural SBP	0.000	0.000	0.000
Postural DBP	0.457	0.494	0.136
Sustained handgrip SBP	0.000	0.000	0.000
Sustained handgrip DBP	0.000	0.000	0.000

* Student's paired-t tests

In Table no.3, Students' paired-t test was used to compare the 2 phases of menstrual cycle at a time, eg: menstrual phase (MP) v/s follicular phase (FP), menstrual phase (MP) v/s luteal phase (LP) and follicular phase (FP) v/s luteal phase (LP).

There was a statistically significant difference of Resting SBP between MP v/s FP, MP v/s LP and FP v/s LP.

The Resting DBP difference between MP v/s FP of menstrual cycle in females is not statistically significant but statistically significant between MP v/s LP and FP v/s LP.

There was a statistically significant difference of Postural SBP between MP v/s FP, MP v/s LP and FP v/s LP.

There was no statistically significant difference of Postural DBP between MP v/s FP, MP v/s LP and FP v/s LP.

There was a statistically significant difference of Sustained handgrip SBP between MP v/s FP, MP v/s LP and FP v/s LP.

There was a statistically significant difference of Sustained handgrip DBP between MP v/s FP, MP v/s LP and FP v/s LP.

DISCUSSION

Resting Blood Pressure: In our study, there was a statistically significant difference in mean systolic blood pressure ($P<0.05$) between all the three phases of the menstrual cycle:– menstrual-follicular, follicular-luteal and luteal-menstrual phases, with higher values in the luteal phase and lower values in follicular phase.

The statistically significant ($P<0.05$) difference in diastolic blood pressure (DBP) was only between two phases:- menstrual-luteal phase and follicular-luteal phase, with higher values in the luteal phase and lower values in follicular phase.

Our results were similar to the study of Garg R *et al*. [7], Kavitha C *et al*. [8], Chakraborty A *et al*. [9] which showed significant increase in the resting systolic and diastolic blood pressure in the luteal phase as compared to the follicular phase and menstrual phase, but contradictory with the study of Arifuddin MS *et al*. [10], Moran VH *et al*. [11] which showed lower values of resting blood pressure in luteal phase.

There exists a significant difference between the SBP in the pre and postmenstrual phase, being higher in the premenstrual phase i.e. luteal phase, which can be explained on the basis of increased salt and fluid retention induced by ovarian steroids and a higher sympathetic nervous system activity [12].

The mean level of SBP varied with the phase of the menstrual cycle, being higher on days 17 to 26 (the part of the luteal phase), during which the peak of progesterone levels develops than during the luteal phase as a whole and significantly higher than the mean for all other days of the cycle[13].

In our study, significant increase in the resting systolic and diastolic blood pressure was observed in the luteal phase as compared to the follicular phase and menstrual phase. The possible causes of decreased blood pressure in the follicular phase may be due to estrogen which causes vasodilatation by stimulating the release of prostacyclin and nitric oxide and inhibit the production of vasoconstrictors like angiotensinogen II and endothelins [14,15]. Estrogen causes smooth muscle relaxation by stimulating the opening of calcium activated potassium channels by nitric oxide and cyclic guanosine monophosphate pathway that causes vasodilatation [16]. Estradiol might also be associated with increase in acetylcholine concentration. These finding suggest that estrogen has facilitating effect on cardio-vagal function [17]. Significant correlations were observed between the plasma oestradiol concentration and the cardiovagal baroreflex sensitivity. The cardiovagal baroreflex sensitivity during the early follicular phase was significantly greater than those of the mid luteal phase and also when compared to men, indicating parasympathetic dominance in the follicular phase[18].

In our study, significant increase in the resting systolic blood pressure was observed in the luteal phase as compared to the menstrual phase may be due to Progesterone, as Progesterone may increase cardiac excitability by its opposing effects on estrogen [19]. Estradiol peaks during luteal phase increase the number and sensitivity of progesterone receptors, thus increasing action of progesterone hormone during luteal phase [19]. Increase level of progesterone causes decreased release of endothelium derived nitric oxide which leads to generalized vasoconstriction and increased BP [20] as level of progesterone is significantly higher in luteal phase, causes rise in both systolic and diastolic blood pressure [21].

Higher resting levels of circulating plasma norepinephrine (a potent vasoconstrictor substance) have been reported during the luteal phase of the menstrual cycle, when both oestrogen & progesterone concentrations are elevated [22]. The plasma renin activity and the concentrations of the fluid regulatory hormones, aldosterone and plasma norepinephrine levels increased along the luteal phase which contributes to the increased cardio-vagal baroreflex sensitivity [23]. Physiological and psychological stress also contributes to the rise in SBP in the premenstrual

phase which is also called as progesterone phase. Also the administration of exogenous progesterone and the combined oral contraceptive pills are known to induce hypertension [13]. This increased action of progesterone hormone during the luteal phase may be responsible for increased sympathetic activity.

In menstrual phase, the concentration of hormones oestrogen & progesterone is low & hence the concentrations of NO & norepinephrine may be low & therefore blood vessel diameter may not be affected & hence the resting blood pressure might have not been affected in the menstrual phase[24]. It has been shown that ovarian steroids in the normal menstrual cycle may alter the autonomic nervous system activity with parasympathetic predominance in the follicular phase and sympathetic dominance in the luteal phase that raises the resting blood pressure [8].

Postural change in Blood Pressure: In our study, changes in blood pressure from supine to standing position showed that there was a statistically significant ($P<0.05$) difference in postural change of systolic blood pressure between all the three phases of the menstrual cycle, with higher fall in luteal phase.

The diastolic blood pressure response to change of posture from supine to standing position showed no statistically significant ($P>0.05$) difference between the three phases of the menstrual cycle, with higher fall in luteal phase.

Our result was similar to the study of Kavitha C *et al*. [8] showed that there was a statistically significant difference in postural change of systolic blood pressure and no statistically significant difference in postural change of diastolic blood pressure between all the three phases of the menstrual cycle.

But not similar with the studies of Chakraborty A *et al*. [9], Agarwal G *et al.* [24] showed a statistically significant difference in postural change of diastolic blood pressure in all the three phases of menstrual cycle.

On sudden changing from supine to standing position, there is peripheral pooling of blood in the dependent parts of the body; this decreases venous return and cardiac output, so the systolic blood pressure which is dependent on left ventricular ejection also decreases. This via the sino-aortic reflex, which operates within seconds, stabilizes the blood pressure.

Study of Hassan AAK *et al*. [25] speculated that the attenuated postural vasoconstriction observed during the luteal phase of ovulatory cycles could result in excessive pooling of blood in the dependent extremities. As a consequence of the greater reduction in the central blood volume, activation of the vasopressin and/or renin-angiotensin-aldosterone system, with a subsequent decrease in urinary volume and urinary sodium excretion might ensue, thus leading to salt and water retention and an aggravation of the oedema state.

The partially impaired postural vasoconstriction during the luteal phase of the menstrual cycle might partly explain the incidence of premenstrual oedema in some women.

The parasympathetic activity is predominant in the follicular phase, resulting in an impairment of baroreflex caused by posture changes. Moreover, baroreflex control of the sympathetic component, not the parasympathetic component increases in the premenstrual phase, while the reflex response of the sympathetic component is less in the ovulatory phase compared with the menstrual or luteal phase concluding that the baroreflex regulation of autonomic functions induced by changing position is modified during the normal menstrual cycle. A difference in the balance of the ovarian hormones along the menstrual cycle may be responsible for these changes of autonomic functions during the menstrual cycle [26].

Therefore, we can conclude that there is an increased postural difference in SBP during the menstrual cycle, with more being in the luteal phase which could be attributed to the increased sympathetic activity in the luteal phase.

Blood Pressure response to Sustained Handgrip: In our study, the systolic and diastolic blood pressure response to sustained hand grip test was statistically significant ($P < 0.05$) between all the phases of menstrual cycle, with higher change in systolic and diastolic blood pressure response to sustained hand grip test in luteal phase.

Our results were similar to the studies of Chakraborty A *et al*. [9], Garg R *et al*. [7] which showed that the systolic and diastolic blood pressure response to sustained hand grip test were statistically significant between all the phases of menstrual cycle in females.

Our results were similar with previous studies of Mehta V *et al*. [12] who reported significantly higher SBP and increased sympathetic activity in luteal phase compared to menstrual and follicular phase.

But not similar with the study of Christina *et al*. [27] who showed no statistically significant result between all the phases of menstrual cycle in females.

When isometric handgrip exercise is performed, there is local collection of chemical substances like lactic acid, adenosine etc. These accumulated metabolites are detected by metabolite-sensitive nerve endings distributed in and around the

skeletal muscle tissue. These substances can increase the discharge of a special type of chemoreceptor called group IV (metaboreceptor) afferent fibers, initiating a potent reflex that increases sympathetic nerve activity. This leads to vasoconstriction, which contributes to the rise in BP [28]. In the menstrual phase, due to reduced progesterone levels, resting blood pressure and the blood pressure response to the tests like isometric handgrip exercise, cold pressor tests and postural challenge test is significantly less than during luteal phase. However, blood pressure in menstrual phase is more than the follicular phase that may be due to fall in estrogen levels [15].

According to Wineman EW [29] the high levels of estrogen in the menstrual cycle are accompanied by decreased sympathetic nervous system activity in follicular phase. Higher estradiol levels have been shown to lower the cardiovascular responses to stress, most likely through an effect on arterial wall tone and a decrease in β-receptor sensitivity to catecholamine.

CONCLUSION

From the result of our study, it can be concluded that blood pressure in the resting state and during the stressful maneuvers like isometric handgrip exercise and standing from lying posture was highest during luteal phase of the menstrual cycle and lowest in the follicular phase. This correlates the higher sympathetic outflow in the luteal phase as compared to the follicular phase and increased parasympathetic outflow in the follicular phase as compared to the luteal phase. This higher sympathetic activity during the luteal phase of the menstrual cycle may be correlated with higher oestrogen & progesterone levels, which may be responsible for premenstrual stress. Further investigations are required to explore the possible biomechanisms underlying our findings.

REFERENCES

1. Parlee MB. Menstrual rhythms in sensory processes: a review of fluctuations in vision, olfaction, audition, taste, and touch. Psychol Bull 1983; 93(3): 539–48.
2. Williams. Pregnancy planning and antepartum management, Text book of Obstetrics. 2006, 22nd ed. P-226.
3. Farage MA, Neill S, MacLean AB. Physiological changes associated with the menstrual cycle: a review. Obstet Gynecol Surv. 2009; 64(1): 58-72.
4. Mishell DR Jr. Premenstrual disorders: epidemiology and disease burden. Am J Manag Care. 2005; 11(16 Suppl): S473-9.
5. Matsumoto T, Ushiroyama T, Kimura T, Hayashi T, Moritani T. Altered autonomic nervous system activity as a potential etiological factor of premenstrual syndrome and premenstrual dysphoric disorder. BioPsychoSocial medicine. 2007 Dec;1(1):24.
6. Reid RL, Yen SS. Premenstrual syndrome. Am I obstet Gynecol 1981; 139: 85-104.
7. Garg R, Malhotra V, Dhar U, Tripathi Y. A study of sympathetic function tests during different phases of menstrual cycle in normal healthy females. J of Evolution of Med and Dent Sci. 2014 Jun 16;3(24):6590-600.
8. Kavitha C, Jamuna BL, Vijayakumar GS. Pressor response during normal menstrual cycle. Int J Biol Med Res. 2012; 3(3): 1975-1981.
9. Chakraborty A, Barman S, Deka J. A study of sympathetic function tests during normal menstrual cycle in young females in the age group of 18-25 years. J Evid Based Med Healthc. 2016; 3(66): 3561-3565.
10. Arifuddin MS, Hazari MA, Reddy BR. Blood pressure variations during different phases of menstrual cycle. International Journal of Science and Nature. 2012 Aug;3(3):551-4.
11. Moran VH, Leathard HL, Coley J. Cardiovascular functioning during the menstrual cycle. Clinical Physiology. 2000 Nov 14;20(6):496-504.
12. Mehta V, Chakrabarty AS. Autonomic functions during different phases of menstrual cycle. Indian journal of physiology and pharmacology. 1993 Jan;37(1):56-8.
13. Greenberg G, Imeson JD, Thompson SG, Meade TW. Blood pressure and the menstrual cycle. BJOG: An International Journal of Obstetrics & Gynaecology. 1985 Oct 1;92(10):1010-4.
14. Everett RB, Worley RJ, MacDonald PC, Gant NF. Modification of vascular responsiveness to angiotensin II in pregnant women by intravenously infused 5α-dihydroprogesterone. American Journal of Obstetrics & Gynecology. 1978 Jun 15;131(4):352-7.
15. Polderman KH, Stehouwer CD, van Kamp GJ, Schalkwijk CG, Gooren LJ. Modulation of plasma endothelin levels by the menstrual cycle. Metabolism-Clinical and Experimental. 2000 May 1;49(5):648-50.
16. Wellman GC, Bonev AD, Nelson MT, Brayden JE. Gender differences in coronary artery diameter involve estrogen, nitric oxide, and Ca2+-dependent K+ channels. Circulation Research. 1996 Nov 1;79(5):1024-30.
17. Du XJ, Dart AM, Riemersma RA. Sex differences in the parasympathetic nerve control of rat heart. Clinical and experimental pharmacology and physiology. 1994 Jun;21(6):485-93.
18. Tanaka M, Sato M, Umehara S, Nishikawa T. Influence of menstrual cycle on baroreflex control of heart rate: comparison with male volunteers. American Journal of Physiology-Regulatory, Integrative and Comparative Physiology. 2003 Nov;285(5):R1091-7.
19. Constantini NW, Dubnov G, Lebrun CM. The menstrual cycle and sport performance. Clinics in sports medicine. 2005 Apr 1;24(2):e51-82.

20. Rosselli M, Imthurm B, Macas E, Keller PJ, Dubey RK. Circulating nitrite/nitrate levels increase with follicular development: indirect evidence for estradiol-mediated NO release. Biochemical and biophysical research communications. 1994 Aug 15;202(3):1543-52.
21. Babyminakshi PL, Mangala KA, Afroz S, Nanda S, Sudhir P. Effect of premenstrual stress on cardiovascular system and central nervous system. J Obstet Gynecol. 2006;56:156-8.
22. Goldstein DS, Levinson P, Keiser HR. Plasma and urinary catechllamines during the human ovulatory cycle. American Journal of Obstetrics & Gynecology. 1983 Aug 1;146(7):824-9.
23. Hirshoren N, Tzoran I, Makrienko I, Edoute Y, Plawner MM, Itskovitz-Eldor J, Jacob G. Menstrual cycle effects on the neurohumoral and autonomic nervous systems regulating the cardiovascular system. The Journal of Clinical Endocrinology & Metabolism. 2002 Apr 1;87(4):1569-75.
24. Agarwal G, Kumar R, Kumar J, Bijaraniya K. Study of Sympathetic Function Tests during Different Phases of Menstrual Cycle. Sch J App Med Sci. 2015;3(3F):1462-6.
25. Hassan AAK, Carter G, Tooke JE. Postrual vasoconstriction in women during the normal menstrual cycle.Clinical Science.1990; 78(1): 39-47.
26. Saeki Y, Atogami F, Takahashi K, Yoshizawa T. Reflex control of autonomic function induced by posture change during the menstrual cycle. Journal of the autonomic nervous system. 1997 Sep 10;66(1-2):69-74.
27. Christina KF, Medabala T, Patil P, Sayana SB. A Comparative Study of Cardiovascular Autonomic Function Tests during Different Phases of Menstrual Cycle.-. International Journal of Health Sciences and Research (IJHSR). 2013;3(6):34-40.
28. Mostoufi-Moab S, Widmaier EJ, Cornett JA, Gray K, Sinoway LI. Forearm training reduces the exercise pressor reflex during ischemic rhythmic handgrip. Journal of applied physiology. 1998 Jan 1;84(1):277-83.
29. Wineman EW. Autonomic balance changes during the human menstrual cycle. Psychophysiology. 1971 Jan;8(1):1-6.