Indian J Physiol Pharmacol 2013; 57(3) : 246–254

CARDIAC AUTONOMIC ACTIVITY IN YOUNG FEMALES WITH PRIMARY DYSMENORRHEA

KIRAN SINGH*[1], DIVYA SRIVASTAVA[1], ARCHANA[1], RAJESH MISRA[1] AND MAMTA TYAGI[2]

Departments of [1]Physiology, [2]Obstetrics and Gynaecology, Subharti Medical College, Meerut – 250 005

(Received on April 17, 2012)

Abstract : Various studies have reported the effect of different phases of normal menstrual cycle on the autonomic control over the cardiac activity using heart rate variability (HRV) analysis. However, information on cardiac autonomic activity in young females suffering from primary dysmenorrhea (PD) is scant. Hence, the aim of the present study was to assess the HRV and blood pressure (BP) in different phases of menstrual cycle in women with PD and to compare these findings with eumenorrheic females. Sixty healthy unmarried female subjects (30 females with PD and 30 control subjects), in the age group of 18-25 years, having regular 28-32 days menstrual cycle were recruited for the study. Anthropometric measurements such as height, weight, BMI and WHR were measured. Blood pressure was measured with automatic blood pressure monitor and lead II ECG recordings were done to obtain HRV, during menstrual, follicular and luteal phases of menstrual cycle in both groups. The data recorded were subjected to time and frequency domain analysis. The results showed that dysmenorrheic women had significantly high BMI ($P<0.05$). Analysis of HRV during the different phases of the menstrual cycle between two groups revealed significantly increased ($P<0.01$) mean HR and significantly reduced ($P<0.01$) mean RR and RMSSD in all the 3 examined phases, SDNN significantly less ($P<0.05$) and systolic BP significantly higher ($P<0.001$) during the luteal phase in study group compared to control. Also, we observed a statistically significant decrease in TP and LF ms^2 ($P<0.05$), HF ms^2 & nu ($P<0.01$) in menstrual phase, HF ms^2 ($P<0.05$) and HF nu ($P<0.01$) in luteal phase, while LF nu and LF-HF ratio were found to be significantly higher ($P<0.01$) in menstrual and luteal phases in women with PD compared to control group. This study has shown decreased HRV in the form of increased sympathetic tone and decreased parasympathetic activity in dysmenorrheic women which may be considered an important cardiovascular risk factor.

Key words : heart rate variability, parasympathetic activity, young females, primary dysmenorrhea, sympathetic activity

*Corresponding author : Dr. Kiran Singh, Professor, Department of Physiology, Subharti Medical College, NH-58, Delhi Haridwar Rd., Meerut – 250005, UP, India; Ph. : 09410886644; E-mail : singhkiran15@yahoo.co.in

INTRODUCTION

Primary dysmenorrhea (PD) is a common gynaecological problem, affecting more than 70% of young women and refers to painful menstrual periods in the absence of any underlying pathology (1). It is characterized by lower abdominal colicky pain which starts with the onset of menstrual flow or a few hours following onset and may last for a few hours up to 2 days. The risk factors for PD are early menarche, long and heavy menstrual flow (2) as well as positive family history (3). Primary dysmenorrhea is seen only in ovulatory cycles usually developing within 6 to 12 months of menarche (4) and peaks in late adolescence and the early 20s (5). The incidence falls with increasing age and with increasing parity (6). Studies suggest that severe menstrual pain is associated with absence from school or work and restricts other activities of daily life (7, 8).

However, the underlying pathophysiological mechanisms of PD remain unknown. Few studies have reported that it may be associated with some degree of autonomic imbalance (9). The sympathetic and parasympathetic branches of the autonomic nervous system (ANS) regulate the activity of the sinoatrial node, the cardiac pacemaker. The beat-to-beat variation in heart rate therefore reflects the time varying influence of the ANS and its components, on cardiac function. Heart rate variability (HRV), a non invasive tool, can assess the balance between sympathetic and parasympathetic regulation on cardiac activity (10). Increased regularity of heart beat activity corresponds to decreased HRV and vice- versa (11). Decreased HRV reflects the increased sympathetic tone or decreased parasympathetic activity and is considered an important cardiovascular risk factor (12).

Various studies have reported greater sympathetic activity in the luteal phase whereas dominant parasympathetic activity in the follicular phase of the menstrual cycle (13, 14, 15). Gonadotropic and ovarian hormones have been known to affect this balance in women (16).

Recent study suggests that primary dysmenorrhea is a significant health problem and may be associated with cardiac arrhythmia especially atrial fibrillation and ventricular arrhythmia (17). Although, many studies have assessed the effect of different phases of menstrual cycle on HRV in eumenorrheic women, there have been very few reports on HRV in dysmenorrheic women. Therefore, the objective of the present study was to assess the HRV in young women suffering from PD and to compare these findings with eumenorrheic women.

MATERIALS AND METHODS

The present study was conducted in the Department of Physiology, Subharti Medical college and associated Chattrapati Shivaji Subharti Hospital, Meerut. The study was approved by the research and ethical committees of the institute. Sixty healthy unmarried female volunteers between the age group of 18-25 years, having regular 28-32 days menstrual cycle for at least last 6 months prior to the study, were recruited from the Subharti University campus and OPD of obstetrics and gynaecology

department. Written informed consent was taken from all the participants prior to the beginning of the study.

The menstrual distress questionnaire (MDQ) was used to assess the physical symptoms associated with the menstrual cycle. The MDQ consisted of 47 items providing eight subcategories of symptoms: pain, concentration, water retention, behavioural changes, autonomic reactions, negative effect, arousal and control (18). All the examined subjects completed the MDQ for the menstrual, follicular and luteal phases of her most recent menstrual cycle. Intensity of pain was assessed by visual analogue scale (VAS). It consists of a horizontal line, 10 cm in length, with the two end points labelled "no pain" and "worst pain". The subject marks on the line at a point that they feel represents their perception of pain. The VAS score in numerical index is determined by measuring the distance in cm from the low end of the line to the point that the subject marks.

The subjects were divided in two groups:

Group I (study) consisting of 30 females suffering from primary dysmenorrhea having VAS score ≥ 4.

Group II consisting of 30 females with few premenstrual symptoms and VAS score ≤ 3 were taken as control.

In the dysmenorrheic group, family history of PD, effect of dysmenorrhoea on daily activity and analgesic requirement was also noted.

Exclusion criteria

After a detailed medical history and thorough clinical examination of the subjects, those with history of secondary dysmenorrhea, premenstrual syndrome, smoking, alcoholism, diabetes, hypertension, thyroid disorders, cardiovascular diseases, taking oral contraceptive pills were excluded from the study.

Experimental protocol

The subjects were asked to report to the research laboratory of the department in the morning between 9-11 AM with following instructions :

i. To avoid food, coffee, tea and strenuous physical activity 2 hours prior to testing

ii. To avoid taking any anti-cholinergic drugs 2 days prior to testing.

Anthropometric measurements

Height was measured by stadiometer to nearest 1 cm and weight by weighing machine (Krups) to the nearest 1 kg with subjects standing without shoes and wearing light clothes. Body mass index (BMI) in kg/m^2 was calculated by Quetelet's index. Circumferences at waist (at the level of umbilicus) and hip (at the level of maximum extension of hips) were measured with a tape measure nearest to 0.1 cm. Waist-Hip ratio (WHR) was calculated.

Recording of blood pressure and HRV

Experiments were done in a quiet room

during which subjects lay supine, awake and breathing normally. Blood pressure and ECG were recorded during the following 3 phases - menstrual phase (M) - 1st to 5th day of bleeding, follicular phase (F) - 6th to 14th day and luteal phase (L) - 15th to 28th day of menstrual cycle. Systolic (SBP) and diastolic blood pressure (DBP) were recorded in the left arm after 10 minute of rest using automatic blood pressure monitor (OMRON HEM -712C, Omron Healthcare, Inc., Illinois, US).

For recording of short term HRV, lead II ECG recordings were done at (25 mm/s & voltage at 10 mm/mV) for 330 seconds to obtain HRV, using data acquisition system, RMS Polyrite D (Chandigarh, India). Recommendation of Task Force on HRV was followed (10).

The ECG signals were converted through a 14-bit A/D converter at a sampling frequency of 256 Hz to PC and were analyzed offline after visual checking of abnormal ECG. High and low filters were set at 99 and 0.1 Hz respectively. The screen sweep speed was kept at 30 mm/sec. HRV software detects the 'R' wave by using tall peak detection algorithm and computes R-R interval. The data recorded was subjected to time domain and frequency domain analysis using the HRV analysis software RMS Polyrite D version 3.0.7 (Chandigarh, India). Frequency domain analysis was performed using non-parametric method of Fast Fourier Transformation.

Time domain indices such as mean RR was measured in seconds, mean heart rate (HR in beats per minute), SDNN (standard deviations of the averages of normal to normal (N-N) intervals), RMSSD (root mean square of differences of successive N-N intervals) and different frequency domain indices such as total power (TP) in absolute values (ms^2), low frequency (LF) component (0.04–0.15 Hz), high frequency (HF) component (0.15–0.4 Hz) in absolute (ms^2) and normalized units (nu) and LF-HF ratio were recorded.

Statistical analysis

SPSS version 11.5 software for windows and Microsoft excel were used for statistical analysis. All values were expressed as mean$\pm$SD. One-way analysis of variance (ANOVA) followed by post-hoc Tukey test was used in analysing the data among the phases of menstrual cycle in both groups. Unpaired Student's t-test was used to find out the level of significance between the two groups. $P<0.05$ was considered statistically significant.

RESULTS

General parameters

In the present study, there was no significant difference ($P>0.05$) with respect to age and WHR between the two groups. Although, the mean BMI was found to be within the normal range in both the groups but on statistical analysis it was significantly higher ($P<0.05$) in dysmenorrheic women compared to control group (Table I). In study group, SBP was significantly higher ($P<0.001$) during luteal phase when compared with menstrual and follicular phases (Table II) and also it was higher ($P<0.001$) in comparison with luteal phase of control subjects (Table IV). However, changes in DBP were not

TABLE I: Age and anthropometric parameters of the subjects of dysmeorrheic (Group I) and eumenorrheic (Group II).

Parameters	*Group I (n=30)*	*Group II (n=30)*	*P value*
Age (years)	19.13±1.27	18.80±0.99	0.265
BMI (kg/m^2)	23.90±4.10	22.08±2.73	0.046*
WHR	0.84±0.05	0.82±0.06	0.236

Values are expressed as Mean±SD; Data was analysed using Student' s unpaired t test.
*(P<0.05) statistically significant. BMI: Body Mass Index; WHR: Waist-Hip Ratio.

significant (P>0.05) amongst all the phases in both groups (Table II and III).

HRV Parameters

Time domain indices

Table II shows comparison of HRV indices among the phases of menstrual cycle in group I. By applying ANOVA, we found no statistically significant differences in mean R-R interval, mean HR, SDNN and RMSSD among the phases of menstrual cycle.

Table III shows HRV indices in different phases of menstrual cycle in Group II. Results of ANOVA showed that mean RR, mean HR and RMSSD differ significantly amongst all 3 phases. When post- hoc test was applied, mean RR and RMSSD were found to be significantly reduced (P<0.001 and P<0.05 respectively) and mean HR was found to be significantly increased (P<0.01) in the luteal phase as compared to the menstrual phase, while SDNN was not significant among all the examined phases.

Analysis of HRV during the different phases of the menstrual cycle between group I and group II (Table IV) showed that mean

TABLE II: Comparison of HRV indices and basal cardiovascular parameters in different phases of menstrual cycle of the subjects of Group I (dysmenorrheic n=30).

Parameters	*Phases of menstrual cycle*			
	M	*F*	*L*	*P value*
Mean RR (s)	0.751±0.08	0.759±0.09	0.716±0.08	0.166
Mean HR (bpm)	81.0±9.29	79.53±8.9	85.40±10.70	0.055
SDNN (ms)	49.15±21.06	47.40±18.63	41.14±16.12	0.148
RMSSD (ms)	35.69±15.95	37.50±17.18	30.33±13.01	0.182
TP (ms^2)	402.15±242.33	470.61±213.95	451.32±304.57	0.568
LF (ms^2)	100.66±77.97	146.72±76.63	124.28±96.15	0.111
HF (ms^2)	87.83±81.56	148.77±127.31	72.53±47.1$^{\#\#}$	0.004
LFnu	57.49±9.88	51.35±12.40	63.20±12.65$^{\#\#}$	0.001
HFnu	42.59±9.74	48.87±12.42	36.79±12.98$^{\#\#\#}$	0.001
LF-HF ratio	1.49±0.70	1.20±0.58	2.11±1.04$^{£\ \#\#\#}$	0.000
SBP (mmHg)	107.50±6.44	107.66±8.27	116.86±8.36$^{£££\#\#\#}$	0.000
DBP (mmHg)	74.20±5.85	73.30±6.63	74.93±4.67	0.550

Values are expressed as Mean±SD; statistical analysis was done by one-way ANOVA test followed by post-hoc Tukey test among 3 phases. The (£) depicts comparison between M & L phases; $^{£}$(P<0.05), $^{£££}$(P<0.001). The (#) depicts comparison between F & L phases; $^{\#\#}$(P<0.01), $^{\#\#\#}$(P<0.001). M-menstrual phase, F-follicular phase, L-luteal phase, Mean RR: mean RR interval, Mean HR (bpm) : mean heart rate in beats per minute, SDNN: standard deviations of averages of normal to normal (N-N) intervals, RMSSD: root mean square of differences of successive N-N intervals, TP: total power in absolute values (ms^2), LF: low frequency and HF: high frequency in absolute values (ms^2) and normalized units (nu), SBP: systolic blood pressure, DBP: diastolic blood pressure.

TABLE III: Comparison of HRV indices and basal cardiovascular parameters in different phases of menstrual cycle of the subjects of Group II (control n=30).

Parameters	*Phases of menstrual cycle*			
	M	*F*	*L*	*P value*
Mean RR (s)	0.866±0.10	0.818±0.06	0.779±0.07$^{£££}$	0.000
Mean HR (bpm)	70.13±8.19	73.66±5.67	77.16±7.35$^{££}$	0.001
SDNN (ms)	55.74±19.25	55.18±17.69	54.51±23.14	0.966
RMSSD (ms)	56.40±23.58	51.07±15.52	43.86±10.16$^{£}$	0.039
TP (ms^2)	562.92±255.10	581.22±279.14	523.66±238.68	0.677
LF (ms^2)	145.21±75.64	161.20±107.87	145.13±117.06	0.780
HF (ms^2)	205.42±102.47	170.97±119.32	120.89±92.95$^{££}$	0.009
LF nu	42.48±11.08	47.91±18.34	54.10±11.11$^{££}$	0.007
HF nu	57.40±10.92	52.02±18.27	45.88±11.10$^{££}$	0.007
LF-HF ratio	0.81±0.36	1.21±0.93	1.30±0.56$^{£}$	0.012
SBP (mmHg)	107.33±6.56	108.93±8.25	109.66±7.14	0.456
DBP (mmHg)	71.06±6.61	71.73±7.91	74.03±7.04	0.252

Values are expressed as Mean±SD; statistical analysis was done by one-way ANOVA test followed by post-hoc Tukey test among 3 phases. The (£) depicts comparison between M & L phases; $^{£}$(P<0.05), $^{££}$(P<0.01), $^{£££}$(P<0.001). M-menstrual phase, F-follicular phase, L-luteal phase, Mean RR: mean RR interval, Mean HR (bpm) : mean heart rate in beats per minute, SDNN: standard deviations of averages of normal to normal (N-N) intervals, RMSSD : root mean square of differences of successive N-N intervals, TP: total power in absolute values (ms^2), LF: low frequency and HF: high frequency in absolute values (ms^2) and normalized units (nu), SBP: systolic blood pressure, DBP: diastolic blood pressure.

TABLE IV: Comparison of HRV indices and basal cardiovascular parameters in different phases of menstrual cycle between two groups (n=30 in each group).

Parameters	*Menstrual Phase*		*Follicular Phase*		*Luteal Phase*	
	Group I	*Group II*	*Group I*	*Group II*	*Group I*	*Group II*
Mean RR (s)	0.751±0.08**	0.866±0.10	0.759±0.09**	0.818±0.06	0.716±0.08**	0.779±0.07
Mean HR (bpm)	81.0±9.29**	70.13±8.19	79.53±8.9**	73.66±5.67	85.40±10.70**	77.16±7.35
SDNN (ms)	49.15±21.06	55.74±19.25	47.40±18.63	55.18±17.69	41.14±16.12*	54.51±23.14
RMSSD (ms)	35.69±15.95**	56.40±23.58	37.50±17.18**	51.07±15.52	30.33±13.01**	43.86±10.16
TP (ms^2)	402.15±242.33*	562.92±255.10	470.61±213.95	581.22±279.14	451.32±304.57	523.66±238.68
LF (ms^2)	100.66±77.97*	145.21±75.64	146.72±76.63	161.20±107.87	124.28±96.15	145.13±117.06
HF (ms^2)	87.83±81.56**	205.42±102.47	148.77±127.31	170.97±119.32	72.53±47.1*	120.89±92.95
LFnu	57.49±9.88**	42.48±11.08	51.35±12.40	47.91±18.34	63.20±12.65**	54.10±11.11
HFnu	42.59±9.74**	57.40±10.92	48.87±12.42	52.02±18.27	36.79±12.98**	45.88±11.10
LF-HF ratio	1.49±0.70**	0.81±0.36	1.20±0.58	1.21±0.93	2.11±1.04**	1.30±0.56
SBP (mmHg)	107.50±6.44	107.33±6.56	107.66±8.27	108.93±8.25	116.86±8.36***	109.66±7.14
DBP (mmHg)	74.20±5.85	71.06±6.61	73.30±6.63	71.73±7.91	74.93±4.67	74.03±7.04

Values are significant; *(P<0.05), **(P<0.01), ***(P<0.001). Mean RR: mean RR interval, mean HR (bpm): mean heart rate in beats per minute, SDNN: standard deviations of averages of normal to normal (N-N) intervals, RMSSD: root mean square of differences of successive N-N intervals, TP: total power in absolute values (ms^2), LF: low frequency and HF: high frequency in absolute values (ms^2) and normalized units (nu), SBP: systolic blood pressure, DBP: diastolic blood pressure.

RR and RMSSD were significantly reduced (P<0.01) and mean HR was significantly higher (P<0.01) in all 3 phases while SDNN was significantly lower (P<0.05) in luteal phase in dysmenorrheic subjects.

Frequency domain indices

In the present study, TP and LF ms^2 showed no statistically significant difference among the three phases of menstrual cycle

in group I (Table II) and group II (Table III). However, significant differences were observed in LF nu, HF (ms^2 and nu) and LF-HF ratio. In dysmenorrheic women, post-hoc analysis revealed significant reduction in HF ms^2 ($P<0.01$) and HF nu ($P<0.001$) and significant increase in LF nu ($P<0.01$) in luteal phase as compared with follicular phase. LF-HF ratio was significantly increased in luteal phase in comparison with menstrual ($P<0.05$) and follicular ($P<0.001$) phases (Table II).

In group II (control), Post-hoc analysis revealed significant reduction ($P<0.01$) in HF (ms^2 and nu) and significant increase in LFnu ($P<0.01$) and LF-HF ratio ($P<0.05$) in luteal phase when compared with menstrual phase (Table III).

Analysis of HRV during the different phases of the menstrual cycle between group I and group II (Table IV), revealed a statistically significant decrease in TP and LF ms^2 ($P<0.05$), HF ms^2 & nu ($P<0.01$) in menstrual phase, HF ms^2 ($P<0.05$) and HF nu ($P<0.01$) in luteal phase, while LFnu and LF-HF ratio were found to be significantly higher ($P<0.01$) in menstrual and luteal phases in women with PD compared to control group.

DISCUSSION

In the present study, we found increased sympathetic activity reflected by decreased total power, increased LFnu and reduced parasympathetic (vagal) tone in the form of decreased SDNN, RMSSD and HF (ms^2 and nu) in the luteal phase compared to follicular phase of the menstrual cycle in both groups. Similar findings have been reported by other authors in normal menstrual cycle (13, 19). Also, significantly higher systolic blood pressure was found in the luteal phase in group I indicating sympathetic dominance.

Earlier studies have shown that there appears to be a correlation between the hormonal levels in female hypothalamo-pituitary-gonadal axis and the ANS control of their cardiac activity (16, 20). Estrogen has a role in increasing vagal and reducing sympathetic activity by enhancing the cholinergic muscarinic activity at central and peripheral levels (21). Elevated progesterone may be responsible for the increase in systolic blood pressure in luteal phase of the menstrual cycle by increasing the fluid and salt retention. Physiological and psychological stress contributes to the blood pressure rise during luteal and menstrual phases. Mehta et al have studied the autonomic functions in the different phases of menstrual cycle and reported significantly higher SBP and increased sympathetic activity in luteal phase compared to menstrual and follicular phases without significant differences in parasympathetic activity (22). One study has reported that, in the menstrual phase, the pain ratings, SBP and DBP were significantly higher in dysmenorrheic group than non dysmenorrheic group and strongly suggests that there is activation of the sympathetic-adrenal-medullary axis by painful stress (23). Little et al also showed higher heart and respiration rates during the luteal phase compared with other phases (24).

In this study, a significant difference was observed between the two groups with respect to their overall HRV status. It was found that the young women with primary

dysmenorrhea had a significantly reduced heart rate variability throughout the menstrual cycle in the form of decreased vagal and increased sympathetic activity reflected by lower total power, HF (ms^2 and nu), SDNN, RMSSD and increased mean heart rate. This is in accordance with the previous study by Hegazi et al (25). In contrast, Matsumoto et al found no differences in HRV between the phases of the menstrual cycle (26).

Further LFnu, which reflects the fluctuation in sympathetic tone and LF-HF ratio, a marker of sympathovagal balance, was found to be increased during menstrual and luteal phases in group I. This suggests that primary dysmenorrhea is associated with shifting of cardiac autonomic activity towards sympathetic dominance along the whole cycle as compared to women with eumennorheic cycle.

The present study showed significantly high ($P<0.05$) BMI in group I compared to the control group, although the mean BMI of the subjects of both the groups was within the normal range. Anthropometric measurements BMI and WHR were used to assess central obesity. Previous studies have reported that central obesity is associated with menstrual disorders (27) and cardiovascular diseases (28).

Our study has limitations. Sample size was small in both groups. HRV was recorded in different phases for one menstrual cycle only. Follow up should be at least for 3 consecutive months. Also, we have not recorded HRV with 24 hours holter monitoring which is a better choice to measure the autonomic activity. Further, the study can be expanded by correlating cardiac autonomic activity with body composition, plasma levels of cortisol, estrogen, progesterone hormones and serum lipid profile and may be extended in obese subjects.

We concluded that women with primary dysmenorrhea have more sensitive responses to the sympathetic-adrenal-medullary axis system than eumennorheic women throughout the whole menstrual cycle. Prospective study is needed to explore the effect of non pharmacological means like slow breathing, as the reports indicate that it decreases the sympathetic nervous system activity (29) and increases the baroreflex sensitivity in normal subjects and patients with heart failure (30).

ACKNOWLEDGEMENTS

We are grateful to Mr. Pankaj and Mr. Rajeev for their technical assistance in the completion of this study.

REFERENCES

1. Dawood M. Primary dysmenorrhea: advances in pathogenesis and management. *Obstet Gynecol* 2006; 108: 428–441.
2. Balbi C, Musone R, Menditto A, Di Prisco L, Cassese E, D'Ajello M, et al. Influence of menstrual factors and dietary habits on menstrual pain in adolescence age. *Eur J Obstet Gynecol Reprod Biol* 2000; 91: 143–148.
3. Unsal A, Ayranci U, Tozun M, Arslan G, Calik E. Prevalence of dysmenorrhea and its effect on quality of life among a group of female university students. *Ups J Med Sci* 2010; 115: 138–145.
4. Avant RF. Dysmenorrhea. *Prim Care* 1988; 15: 549–559.
5. Fraser IS. Prostaglandins, prostaglandin

inhibitors and their roles in gynaecological disorders. *Baillieres Clin Obstet Gynaecol* 1992; 6: 829–857.

6. Andersch B, Milsom I. An epidemiologic study of young women with dysmenorrhea. *Am J Obstet Gynecol* 1982; 144: 655–660.
7. Ylikorkala O, Dawood MY. New concepts in dysmenorrhea. *Am J Obstet Gynecol* 1978; 130: 833–847.
8. Burnett MA, Antao V, Black A, Feldman K, Grenville A, Lea R, et al. Prevalence of primary dysmenorrhea in Canada. *J Obstet Gynecol Can* 2005; 27: 765–770.
9. Kim E, Cho JH, Jung WS, Lee S, Pak SC. Effect of acupuncture on heart rate variability in primary dysmenorrheic women. *Am J Chin Med* 2011; 39: 243–249.
10. Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology Heart rate variability: standards of measurement, physiological interpretation, and clinical use. *Circulation* 1996; 93: 1043–1065.
11. Gang Y, Malik M. Heart rate variability analysis in general medicine. *Indian Pacing Electrophysiol J* 2003; 3: 34–40.
12. Kleiger RE, Miller JP, Bigger JT, Moss AJ. Decreased heart rate variability and its association with increased mortality after acute myocardial infarction. *Am J Cardiol* 1987; 59: 256–262.
13. Shetty S, Pai SR, Nayanatara AK, Ramesh BM, Shetty BA. Comparative study of time and frequency domain indices of spectral HRV analysis in different phases of menstrual cycle. *J Chin Clin Med* 2010; 5: 469–473.
14. Sato N, Miyake S, Akatsu J, Kumashiro M. Power spectral analysis of heart rate variability in healthy young women during the normal menstrual cycle. *Psychosom Med* 1995; 57: 331–335.
15. Yildirir A, Kabakci G, Akqul E, Tokqozoqlu L, Oto A. Effects of menstrual cycle on cardiac autonomic innervation as assessed by heart rate variability. *Ann Noninvasive Electrocardiol* 2002; 7: 60–63.
16. Chatterjee S, Aditya S, Tibarewala DN. A Comparative study between females of pre-pubertal and reproductive age groups to explore how HPG-Axis affects the autonomic control over cardiac activity. *Indian J Biomech* 2009; 233–236.
17. Bilir C, Akdemir N, Colak D, Cinemre H. Electrocardiographic findings in patients with primary dysmenorrhea. *Am J Med Sci* 2012; 343: 27–29.
18. Moos RH. The Menstrual Distress Questionnaire. *Psychosom Med* 1968; 30: 853–867.
19. Ghildiyal A, Iqbal B, Singh S, Verma D, Singh S. Changes in sympathovagal balance during menstural cycle. *Current Neurobiol* 2011; 2: 49–52.
20. Leicht AS, Hirning DA, Allen DA. Heart rate variability and endogenous sex hormones during the menstrual cycle in young women. *Experiment Physiol* 2003; 88: 441–446.
21. Du XJ, Riemersma RA, Dart AM. Cardiovascular protection by oestrogen is partly mediated through modulation of autonomic nerve function. *Cardiovasc Res* 1995; 30: 161–165.
22. Mehta V, Chakrabarty AS. Autonomic function during different phases of menstrual cycle. *Indian J Physiol Pharmacol* 1993; 37: 56–58.
23. Park M, Watanuki S. Specific physiological responses in women with severe primary dysmenorrhea during the menstrual cycle. *J Physiol Anthropol Appl Human Sci* 2005; 24: 601–609.
24. Little BC, Zahn TP. Changes in mood and autonomic functioning during the menstrual cycle. *Psychophysiology* 1974; 11: 579–590.
25. Hegazi M, Nasrat H. Heart rate variability in young healthy females with primary dysmenorrhea. *Bull Alex Fac Med* 2007; 43 no 3.
26. Matsumoto T, Ushiroyama T, Morimura M, Moritani T, Hayashi T, Suzuki T, et al. Autonomic nervous system activity in the late luteal phase of eumenorrheic women with premenstrual symptomatology. *J Psychosom Obstet Gynecol* 2006; 27: 131–139.
27. Douchi T, Kuwahati R, Yamamoto S, Oki T, Yamasaki H, Nagata Y. Relationship of upper body obesity to menstrual disorders. *Acta Obstet Gynecol Scand* 2002; 81: 147–150.
28. Ribeiro–Filho FF, Faria AN, Kohalmann O Jr, Ajzen S, Ribeiro AB, Zanella MT, et al. Ultrasonography for the evaluation of visceral fat and cardiovascular risk. *Hypertension* 2001; 38: 713–717.
29. Pepper E, Crane-Gockley V. Towards effortless breathing. *Medical Psychotherapy* 1990; 3: 135–140.
30. Joseph CN, Porta C, Casucci G, Casiraghi N, Maffeis M, Rossi M, et al. Slow breathing improves arterial baroreflex sensitivity and decreases blood pressure in essential hypertension. *Hypertension* 2005; 46: 714–718.