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Research Article

INFLUENCE OF DIFFERENT PHASES OF MENSTRUAL CYCLE ON HEART RATE VARIABILITY

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ABSTRACT
The female menstrual cycle is characterized by monthly rhythmical changes in the rates of secretion of female hormones which effect the cardiac autonomic function. Heart rate variability (HRV) is an indirect noninvasive measure of the cardiac autonomic function. This study shows the influence of different phases of menstrual cycle on cardiac autonomic regulation. The frequency domain analysis of HRV was determined for 60 normally menstruating young females in the age group of 18-30 years in their follicular and luteal phases of the menstrual cycle. There is an increase in the low frequency (LF) domain and a decrease in the high frequency (HF) domain with a subsequent increase in the LF/HF ratio in the luteal phase of the menstrual cycle when compared to the follicular phase though statistically non-significant. Sympathetic nervous activities are predominant in the luteal phase as compared to the follicular phase of the menstrual cycle.

Keywords: *Menstrual Cycle, Heart Rate Variability (HRV), Low Frequency Domain (LF), High Frequency Domain (HF)*

INTRODUCTION
Menstruation is the cyclic, orderly sloughing of the uterine lining on account of the interactions of hormones produced by the hypothalamus, pituitary, and ovaries. The hypothalamus, pituitary and ovaries form an endocrine axis (known as the HPO axis) that functions via hormonal regulation and feedback loops and it is this system that governs the regulation of menstruation. Ovarian hormones alterations along the menstrual cycle are associated with corresponding significant changes in multiple neurohumoral homeostatic mechanisms regulating the cardiovascular system (Hirshoren *et al.,* 2002).
The menstrual cycle is thus is associated with variations in endocrine fluctuations and the associated metabolisms. Amongst the various studies conducted on the changes in different systems during the menstrual cycle, a number of studies have emphasized on the cardio respiratory changes during menstrual cycle, thereby depicting the changes on the heart and respiratory system. Some previous studies reported a sympathetic predominance in the luteal phase (Sato *et al.,* 1995), whereas others reported vagal predominance in the luteal phase (Princi *et al.,* 2005).
HRV is reflective of the general wellness state of the organism. It is generally studied as the variation over time of the period between consecutive heart beats, and; is predominantly dependent on the extrinsic regulation of the heart rate. HRV is thought to reflect the heart's ability to adapt to changing circumstances by detecting and quickly responding to unpredictable stimuli. HRV analysis's ability to assess overall cardiac health and the state of the ANS responsible for regulating cardiac activity underlies in its promise as a major new tool in the diagnostic and monitoring armamentarium (Chatterjee *et al.,* 2009).
In the spectral analysis of HRV, the frequency domain parameters include High frequency (HF) component - 0.15- 0.40 Hz, Low frequency (LF) – 0.04- 0.1 Hz & LF /HF ratio.
The HF component measures the parasympathetic modulation of SA node through vagus, whereas LF component provides the index of sympathetic effects on the heart; while LF / HF ratio indicates sympathovagal balance. Decreased HRV reflects the increased sympathetic tone or decreased parasympathetic activity and is considered an important cardiovascular risk factor (Task Force of The European Society of Cardiology and The North American Society of Pacing and Electrophysiology

1996). Heart rate variability (HRV) in women has been related independently to endogenous sex hormones, hormone replacement therapy, menopause, menstrual cycle, body mass index (BMI), and physical conditioning. HRV has proved to be a more sensitive tool for the detection of autonomic balance than mean heart rate (Shetty *et al.*, 2011).Hormonal factors may be a cause of variance in HRV tests among young adult males and females (Liu *et al.*, 2003).

Therefore this study is conducted to measure the changes in the cardio autonomic parameters during menstrual cycle.

MATERIALS AND METHODS

To study the cardiac autonomic activity, using HRV, during different phases of menstrual cycle, a total of 60 healthy females aged 18-30 years, who were eumenorheic i.e. having regular normal menstrual cycles of 28-40 days and normotensive (<140/90 mmHg) were selected and the study was conducted in the Department of Physiology, M.R. Medical College, Gulbarga.

Those with a history of irregular cycles, menorrhagia, neurological disorders, postural symptoms or syncopal attacks or intake of any medication including oral contraceptive pills and subjects with known respiratory, cardiovascular illness, or any disorder which can interferewith the autonomic responses were excluded from the study.

Informed written consent was obtained from each subject after explaining the procedure. All the subjects were given a prepared questionnaire to answer. A detailed clinical history, including socio-demographic data, name and age was taken.A complete general physical examination, including anthropometrical measurements and systemic examination was conducted in all subjects.

The phase of the cycle on entry was calculated from the date of onset of the last menstrual period. Each subject was studied for six weeks, during which time at least one full menstrual cycle was completed.

Recordings of cardiac autonomic activity were made on specified days of a single menstrual cycle, in two phases:

- Follicular phase – day 4 to day 14
- Luteal phase – day 15 to day 28

The ECG was recorded using ADInstruments–PowerLab ® /30 Series. The PowerLab is essentially a device specifically designed to perform the various functions needed for data acquisition, signal conditioning and preprocessing. It contains its own microprocessor and specialized analog amplifiers for signal conditioning.

Skin surface was cleaned with alcohol swabs and Gel was applied to both wrists and right foot. Red Electrode (-ve electrode) was placed over right wrist, black electrode (+ve electrode) was placed over left wrist and the green electrode (earth) was placed over right foot in supine position. These Electrodes were connected to ADInstruments Bio Amp.

Students were instructed to remove metallic possessions like ornaments, watch etc.They were asked not to move their limbs during recording. ECG Recording was taken for 5 min in supine position with eyes closed and with the subject breathing normally at the rate of 12- 18 breaths per minute. The HRV analysis for frequency domain (LF, HF & LF/HF) was done.

The data was expressed in mean ± SD. Students paired *t* test used for statistical analysis. Statistical software namely SPSS 18 version was used for the analysis of the data

RESULTS AND DISCUSSION

Table 1: Anthropometric Details of Study Participants

n = 60	**Mean ±SD**
Age (years)	21.085 ± 2.90
Weight (kg)	55.96 ± 4.79
Height (m)	1.521 ± 0.06
BMI (kg/m^2)	24.184 ± 3.531

The above table shows the anthropometric details of the study group comprising of 60 young adult females having a mean age of 21.085 ± 2.90 years and mean weight of 55.96± 4.79 and mean height of 1.521 ± 0.06 m. The mean BMI was found to be 24.184± 3.531 kg/m^2.

Table 1: Comparison of HRV in Follicular & Luteal Phase of Menstrual Cycle

HRV (%)	Follicular Phase (Mean±SD)	Luteal Phase (Mean±SD)	t value	p value
Low frequency (LF)	39.752±20.40	41.684±20.19	t - 0.5215	p>0.05
High frequency (HF)	51.20±16.06	47.218±15.57	t- 1.379	p>0.05
LF/HF ratio	0.899±0.617	1.03±0.705	t- 1.083	p>0.05

It was observed that there was an increase in the LF domain and LF/HF ratio of HRV and a decrease in HF domain in the luteal phase when compared to the follicular phase of the menstrual cycle, but the difference is statistically non significant (p > 0.05).

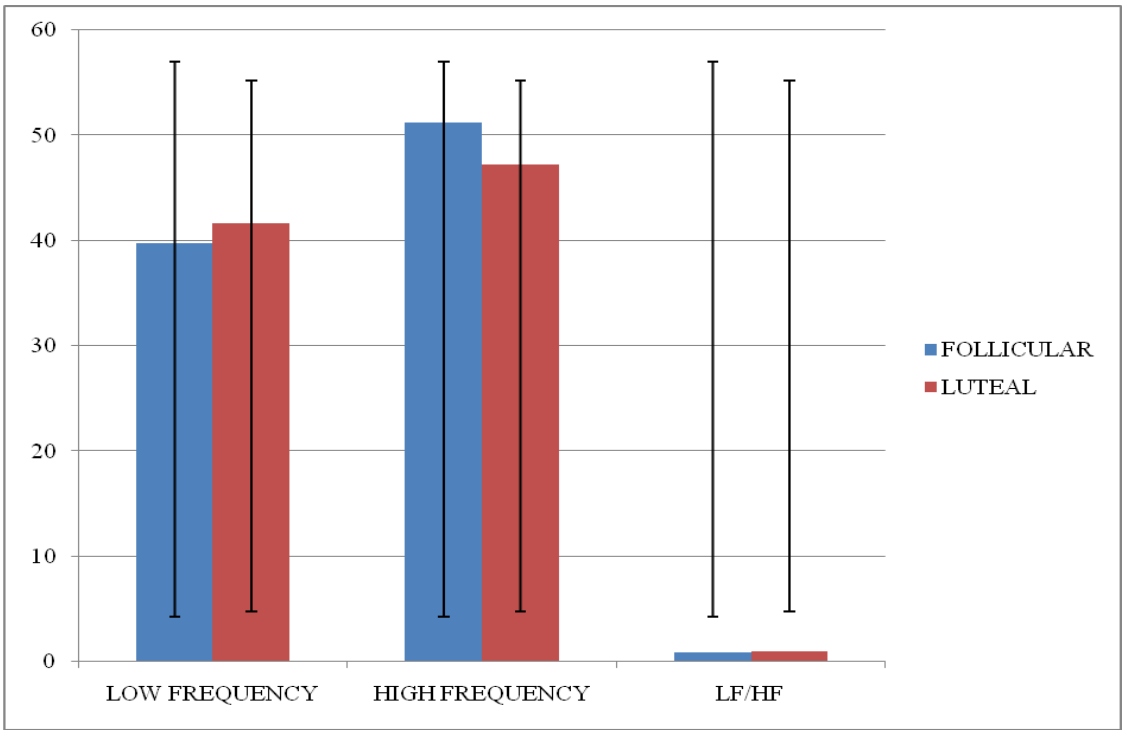

Figure 1: Comparison of HRV in Follicular & Luteal Phase of Menstrual Cycle

The sympathovagal balance in women is affected by gonadotropic (FSH and) and ovarian hormones (estrogen and progesterone) with evidences showing that estrogen has an impact on various metabolic systems in the body. Estrogen is a sympathoinhibitor and vagotonic while progesterone attenuates sympathetic baroreflex responses via a central mechanism (Carr, 2003, Fu *et al.*, 2008).

Estrogen exerts antiarrhythmic effects, possibly by acting on the L-type Ca^{2+} channels, contributing to its cardio protective actions (Nakajima *et al.*, 1999) and can also up regulate the sodium-calcium exchanger (NCX1) through a genomic mechanism mediated by estrogen receptors (ER), contributing to the enhanced propensity to early after depolarizations in female hearts (Sheng *et al.*, 2011).

In the present study LF and LF/HF ratio were increased in luteal phase when compared to follicular phase of the menstrual cycle however the differences were not statistically significant
($p > 0.05$). The increase in sympathetic activity in luteal phase may be due to the higher progesterone level, as progesterone inhibits the influence of estrogen on cardio-vagal activity (Shetty *et al.,* 2011, Tanaka *et al.,* 2003).
The HF was decreased in luteal phase when compared to follicular phase but the differences were not statistically significant ($p > 0.05$). This may be due to the increased endogenous oestrogen levels which causes enhanced vagal activity at ovulation leading to increase in HF i.e. increase in parasympathetic activity in follicular phase (Sato *et al.,* 1995, Rani *et al.,* 2013).
Similar findings were observed in studies done by Leicht *et al* (2003) and Matsumoto *et al.,* (2007) which revealed that LF and LF/HF ratio was increased in luteal phase while HF was increased in follicular phase but the differences were not statically significant.
Sato *et al.,* (1995) found that the vagal activity increased only during the follicular phase as evidenced by lower LF nu and LF/HF ratio, greater HF nu, when compared with other phases of the menstrual cycle. There was significant association between HRV and vagal activity in the follicular phase and concluded that parasympathetic nervous activities are predominant in the follicular phase when compared with the luteal phase.
Similarly, Guasti *et al.,* (1999), Yildirir *et al.,* (2002) reported greater sympathetic activity only during the luteal phase which was statistically significant, indicating that sympathetic activity is predominant in luteal phase.
While Princi *et al.,* (2005) reported greater levels of high frequency (HF) during the luteal phase i.e. greater cardiac parasympathetic modulation during the luteal phase compared to follicular phase of menstrual cycle.
Studies indicate that vagal activity may be greater during the early follicular phase of the menstrual cycle and subsequently lower at other phases of the menstrual cycle, possibly due to the influences of increasing levels of FSH and LH (ovulation phase) and progesterone (ovulation and luteal phases).
However study done by Leicht *et al.,* (2003) demonstrated no synchronistic changes in HRV with endogenous female sex hormone levels at the three main phases of the menstrual cycle. Possible inhibitory influences of FSH, LH and progesterone on oestrogen could account for the lack of oestrogen-induced increased HRV and vagal activity during the menstrual cycle.
Also correlations between oestrogen and HRV at ovulation provided further support of the reported cardio-protective effects of oestrogen.
Thus the variations in hormones during the menstrual cycle alter the cardiac autonomic activity as reflected by HRV parameters.
From the above study it can be concluded that the regulation of autonomic tone is modified during the normal, regular menstrual cycle. Any alteration in menstrual cycle due endogenous reproductive hormone imbalance, as seen in many gynecological disorders, may lead to sympathetic over activity and sympathovagal imbalance and, thus increasing the chances of cardiac autonomic dysfunction, ultimately leading to cardiovascular diseases in females. Also the phase of menstrual cycle should be taken into account when evaluating HRV among women in reproductive age in order to improve interpretation in clinical settings and in future research.

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