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RESEARCH ARTICLE

ESTROGEN LOWERS HEART RATE IN PRE-OVULATORY PHASE OF MENSTRUAL CYCLE IN WOMEN

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Abstract

Hormonal fluctuation in various phases of menstrual cycle may be an important regulatory factor of heart rate. Based on this proposition, an observational study was conducted in 81 women with normal reproductive health to find out the changes of heart rate in the pre-ovulatory (10-13th day of menstrual cycle) and post-ovulatory phases of menstrual cycle. Data were analyzed using Pearson correlation and paired t-test. The test for correlation coefficient using t-statistics showed that the changes of heart rate between pre-ovulatory and post-ovulatory phases was statistically significant ($r= 0.79$, $R^2=0.63$ and $p<0.01$). On the other hand, the paired t-test (2 tails) revealed that the heart rate was significantly decreased ($t= 3.86$, $df=80$, $M_d=3.04$ and $p<0.01$) in the pre-ovulatory phase when compared to the post-ovulatory phase. It is well documented that both estrogen and progesterone level are found to have moderate in luteal phase in relation to the pre-ovulatory phase during LH surge or peak estrogen level and it is approximately 10 times just 10-12 hours before ovulation. From the endocrinological view point, it can be concluded that the estrogen may have the heart rate lowering effects in pre-ovulatory phase in the study subjects.

Introduction:-

Menopause and pregnancy-induced hypertension is very common in some cases, but the variations in blood pressure (BP), heart rate (HR) and other cardiovascular parameters during menstruation are not properly documented, and the available reports regarding this issue are very much contradicting till date.

Blood pressure (BP) & heart rate (HR) are two major parameters of cardiovascular functions of the body which can be modulated by variations of reproductive hormones primarily estrogen throughout the menstrual cycle **(Cunningham et al. 2010),** because treatment with estrogen promotes vasodilation not only in humans, but also in experimental animals by means of stimulation of biosynthesis of prostacyclin and NO by endothelial NO synthase **(Cambliss & Shaul, 2002 and Hernandez et al., 2000).**

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Throughout the menstrual cycle, endogenous sex hormones levels fluctuate regularly. While progesterone and oestrogen are both increased during the mid-luteal phase, oestrogen increases gradually during the follicular phase (**Yazar and Yazici, 2016, Baird and Fraser, 1974 and Carr and Wilson, 1987**).

The heart rate and blood pressure are the most common and easily measurable indices of cardiovascular parameters. While some studies **(Hassan et al., 1990, Kaplan et al., 1990, and Manhem & Jern, 1994)** have found an increase in basal heart rate during the post-ovulatory phase, other studies have not found any effects of the menstrual cycle on heart rate while at rest (**Girdler et al., 1993 and Sato et al., 1998)**.

These variations in findings are attributed to the difficulties in the methodology originating from reliance upon small number of study subjects. To overcome this problem we have rigorously studied the changes of heart rate throughout the course of menstrual cycle of 81 women participants.

Materials and Methods:-

An observational study was conducted among 81 apparently healthy and willing women aged between 18-35 years with regular menstrual cycle of 28 days duration at Kalyani Municipality area of the district Nadia, West Bengal, India. The subjects were regularly monitored and interviewed on different days of interest across menstrual cycle using predesigned questionnaire to collect data regarding heart rate and others.

From the endocrinological view point, each phase of menstrual cycle shows a specific characteristic features due to hormonal, structural and functional changes of various part of female reproductive system during menstrual cycle **(Baird Fraser, 1974, Hoff et al., 1983, Filicori et al., 1984, and Carr and Wilson, 1987)**. So, heart rate was recorded once in the morning (between 10:00am to 1:00pm) in different phases of menstrual cycle.

The exclusion criteria for the participants were pregnancy, irregular menstrual cycle, menorrhagia, had any endocrine disorder or were on any regular medication or oral contraceptive pills.

For the sake of convenience of the study, the menstrual cycle is divided into two phases i.e., pre-ovulatory phase just 2-3 days before ovulation (i.e., after 10 days of menstruation or 11-13 days of menstrual cycle) when estrogen level was found to have maximum and post-ovulaory or luteal phase (15-27th day of menstrual cycle) when both estrogen and progesterone level is maintained to moderate level.

In this study, the menstrual cycle is divided into pre-ovulatory phase during follicular development just 1-3 days before ovulation and the luteal or secretory phase after ovulation. The LH surge is started by a dramatic rise of estradiol secreted by pre-ovulatory graffian follicles and resulting subsequent ovulation. The LH surge is responsible for the leutinization of the granulose cells and stimulates the biosynthesis of progesterone resulting FSH surge **(Reed and Carr, 2018)**.

Data were expressed as average ± SEM and analyzed by Pearson correlation and paired-t test at both 5% and 1% level of significance using both SPSS 20.0 and Stats Tester 4.0.1 software, BPM group Saitama, Japan.

Results:-

The present study tested the changes of heart rate in pre-ovulatory and post-ovulatory phases of the reproductive cycle of the young female subjects with normal reproductive health those who have regular 28 days of menstrual cycle.

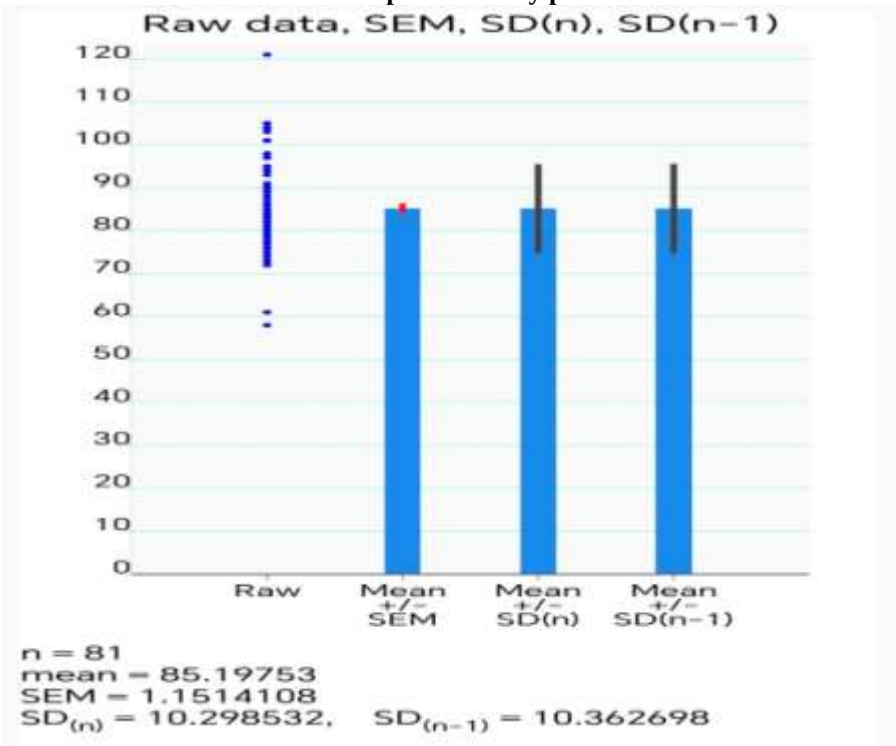
The age and heart rate of the participants in pre-ovulatory and post-ovulatory phases of menstrual cycle were depicted in the table-1 as average ± SEM. The descriptive statistics **(Table-1 & Fig.-1 A & B)** showed that the mean age of the study subjects was 27.35 years. On the other hand, average heart rates in pre-ovulatory and luteal phases were 85.19 and 88.28 beats per minutes (bpm) respectively. Therefore, the mean HR in luteal phase increased 3.05 beats per minute (bpm) in relation to the pre-ovulatory phase.

This increase of heart beats in post-ovulatory phase was tested using Pearson correlation coefficient (linear regression) and paired t-test. The subjects-specific correlation and linear regression **(Fig.-2A)** analysis revealed that there was a correlation ($r=0.7943$, $R^2 = 0.6309$) between HR of pre-ovulatory and post-ovulatory phases and this

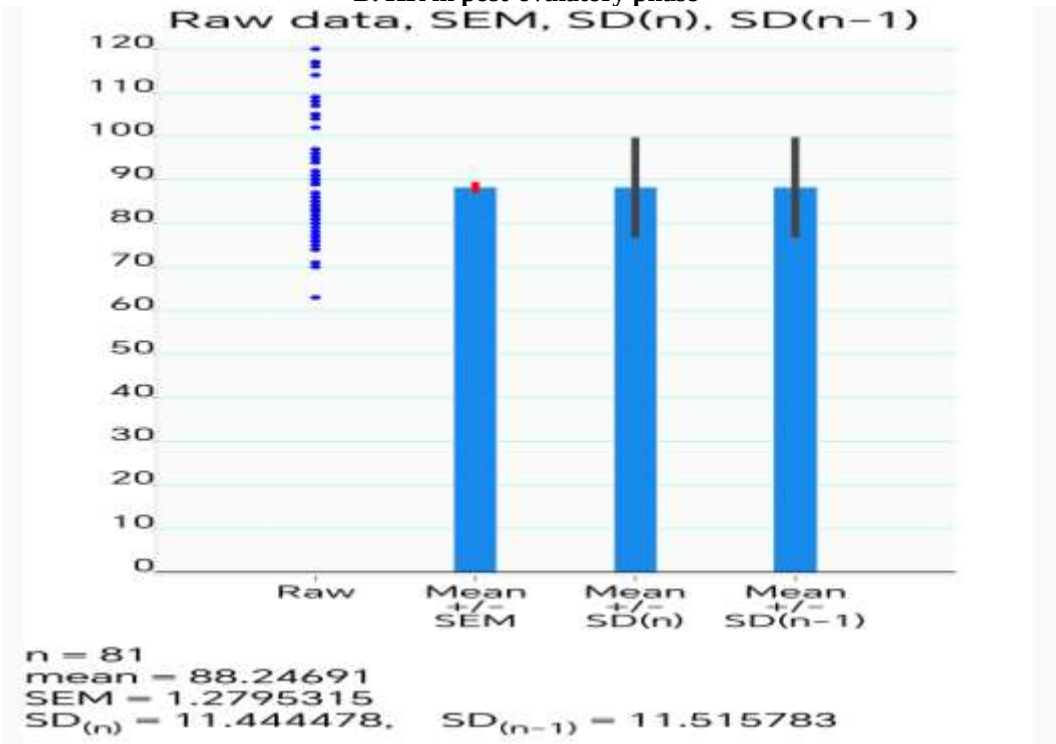
correlation is significant (t=11.62, df=79, r=0.7943 and p<0.01) in this study. On the other hand, two tails paired t-test **(Fig-2B)** showed that this changes of HR is significantly (t=3.86, df=80, M_d= 3.049, SEM of difference = 0.7889 and p<0.01) decreased in pre-ovulatory phase compared to the luteal phase.

Fig 1:- Descriptive statistics about heart rate in pre-ovulatory and post-ovulatory phases of menstruation.

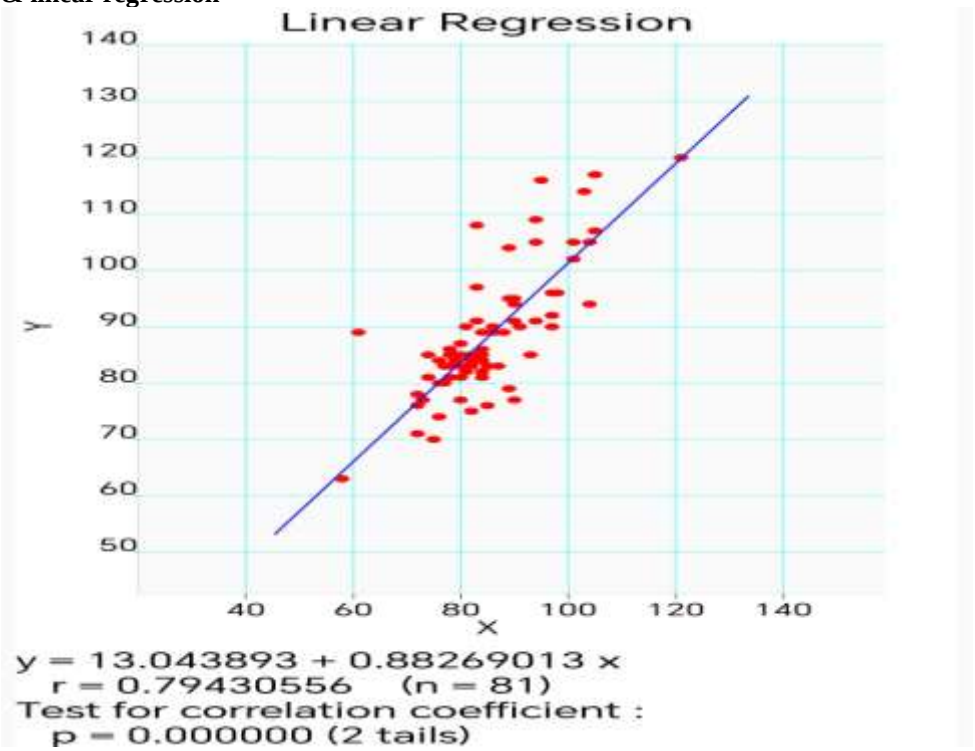
A. HR in pre-ovulatory phase



B. HR in post-ovulatory phase



Correlation & linear regression



B. Paired t-test

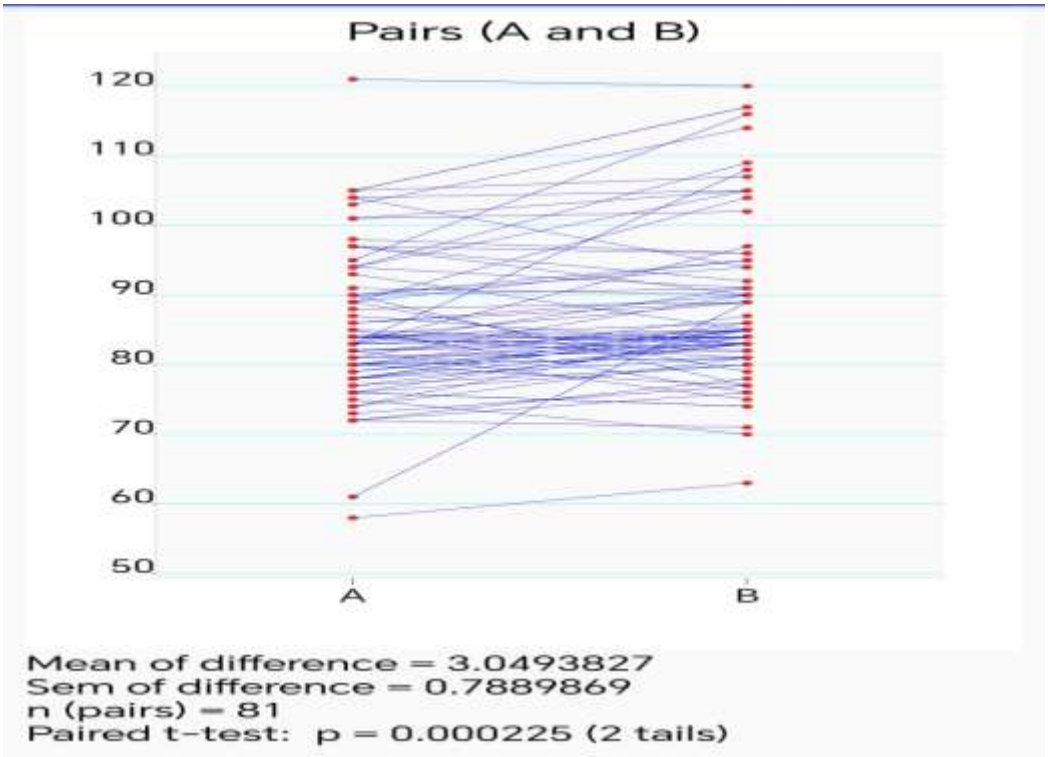


Fig. 2:- HR changes in the pre-ovulatory and luteal phases A: Subjects-specific correlation and linear regression line B: Paired t-test showing individual line for each pair of subjects.

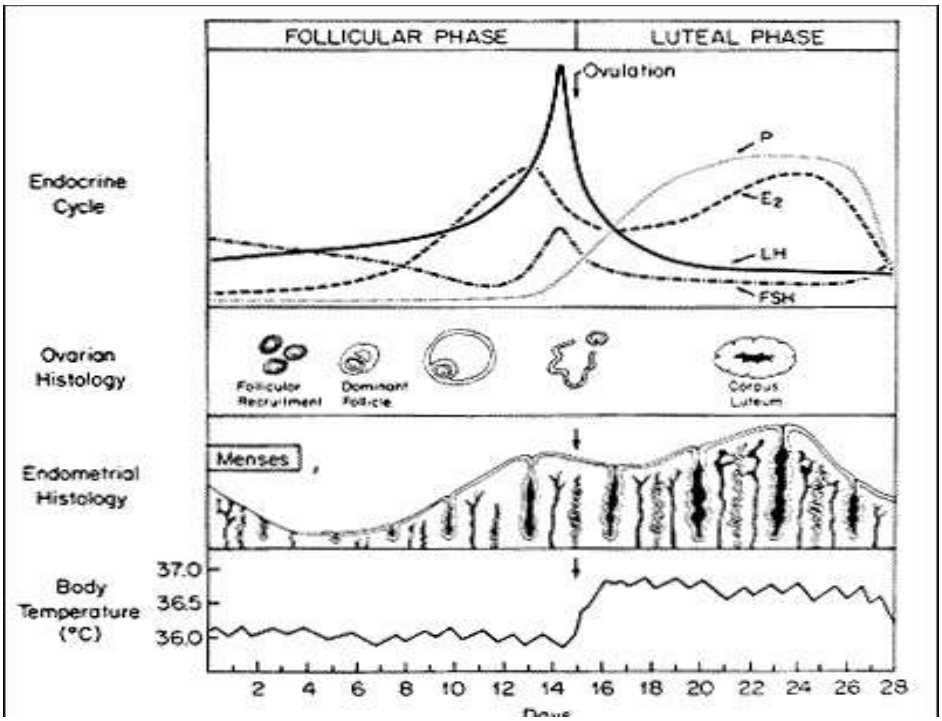


Fig. 3:- Hormonal, endometrial, ovarian and basal body temperature changes across normal menstrual cycle (Carr and Wilson, 1987).

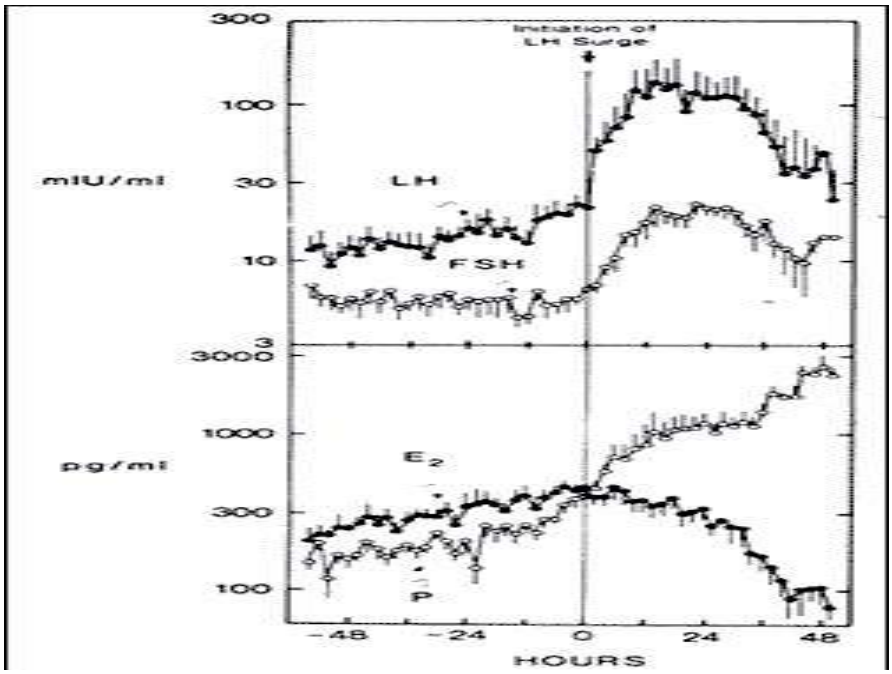


Fig. 4:- LH surge starts 36 hrs before ovulation and usually peak just 10-12 hrs before ovulation (Hoff et al., 1983).

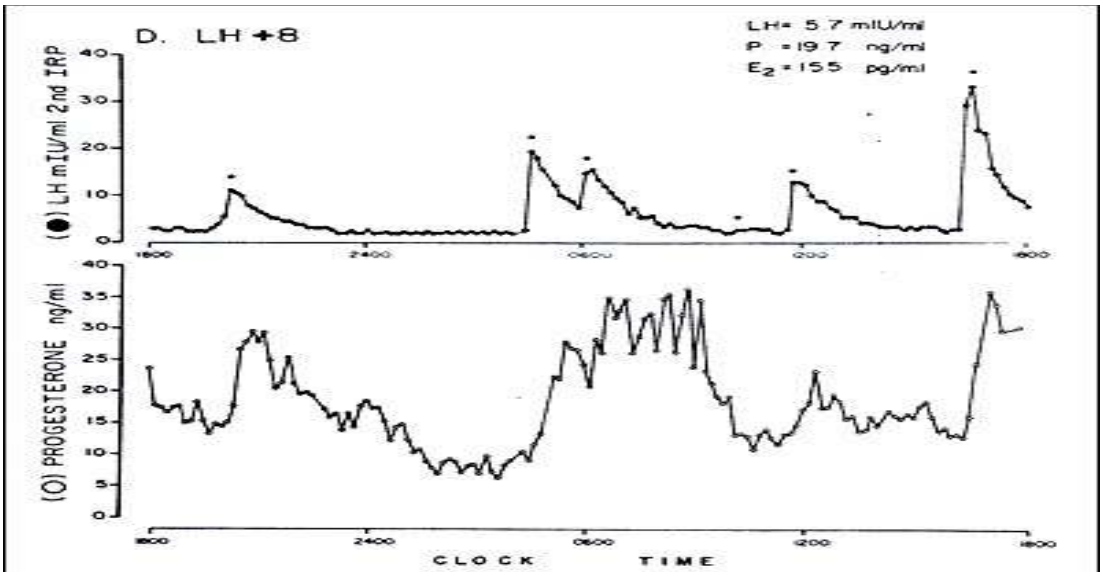


Fig. 5:- Episodic secretion of LH (top) and progesterone (bottom) during the luteal phase of menstrual cycle (Filicori et al., 1984).

Table 2:- Level of sex steroids in women at different phases of menstrual cycle (Baird and Fraser, 1974).

Sex steroids	Early follicular phase	Pre-ovulatory phase	Mid-luteal Phase
Progesterone (mg)	1.0	4.0	25.0
17α-hydroxyprogesterone (mg)	0.5	4.0	4.0
DHEA (mg)	7.0	7.0	7.0
Androstenodione (mg)	2.6	4.7	3.4
Testosterone (µg)	144	171	126
Estrone (µg)	50	350	250
Estradiole (µg)	36	380	250

Table 1:- Mean age and the HR in pre-ovulatory & luteal phases of menstrual cycle of the participants .

Age of participants (Years) Mean±SEM (n=81)	**HR in Pre-ovulatory phase (bpm)** Mean±SEM (n=81)	**HR in Post-ovulatory phase (bpm)** Mean±SEM (n=81)
27.35±0.79	85.19±1.15	88.24± 1.27

Discussion:-

The results demonstrated that HR is significantly higher in the luteal phase and it may be due to moderate level of estrogen. This kind of study was also observed by some workers where basal heart rate is significantly peaked in the luteal phase when compared to other phases of reproductive cycle **(Hassan et al., 1990 and Kaplan et al., 1990),** although the ovulatory phase was not distinguished in those studies.

The level of sex steroids and gonadotropic hormones in different phases of menstrual cycle were well studied in previous works where it was found that the level of estrogen is started to increase 36hrs before ovulation and it is peak just 10-12hrs before during LH surge and then it is maintained to moderate level at luteal phase **(Baird and Fraser, 1974, Hoff, et al., 1983, Filieori et al., 1984, Carr and Wilson, 1987)**. Many studies shows that the estrogen acts as a cardioprotective hormone in women (**Du Xiang et al., 2021**). As heart rate is one of the key

indicator of cardiac functions, the high estrogenlevel in the pre-ovulatory phase may be an important regulator of heart beat in the study subjects.

According to **Giraud et al. (1990),** the increases can be ascribed to one of two mechanisms: either oestrogen increases blood volume (peaking during ovulation and lasting for 10–13 days later were shown in the study of **Baird and Fraser, 1974** and **Carr and Wilson, 1987**), or it enhances sympathetic cardioacceleration (via the same mechanism that increases vasoconstriction **(Leathard & Eccles, 1991).** However, it is also possible to understand the luteal phase-induced basal heart rate as a reflex reaction to a drop in systolic blood pressure. It will take more investigation to distinguish between these possibilities.

Some other previous reports also support our study where HR increases **(McKinley, 2009 and Girija & Veeraiah, 2011)** and SDNN during heart rate variability (HRV) test decreases when examining 2 data points in the follicular phase **(McKinley et al., 2009)**. However, other studies have failed to find out any changes in HR across the menstrual cycle **(Sato et al., 1995; Tousignant-Laflamme & Marchand, 2009, Yildirir et al., 2002)** while some shows that SDNN is elevated in later menstrual phases **(Vallejo et al., 2005)**.

The previous works were done taking few participants because it is very much difficult to day-to-day monitoring of different phases of menstrual cycle. That is why, the present study was rigorously completed on 81 young women with normal reproductive health which offers more comprehensive study on HR changes in pre-ovulatory and post-ovulatory phases.

Conclusion:-

This study inferred that the HR is significantly decreased in the pre-ovulatory phase especially during LH surge or peak level of estrogen in comparison to the luteal phase. From the endocrinological aspect, it can also be concluded that the decreased heart rate in the pre-ovulatory phase just 1-3 days before ovulation may be due to peak level of estrogen in the pre-ovulatory phase in comparison to the luteal phase.

Conflicts of Interest:

There is no conflict of interest declared by the authors.

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Bibliography:-

1. Baird, D.T., and Fraser, I.S. (1974). Blood production and ovarian secretion rates of estradiole-17β and estrone in women throughout the menstrual cycle. J Clin Endocrinol Metab38, 1009-1017.
2. Cambliss, K.L., and Shahul, P.L. (2002). Rapid activation of endothelial NO synthase by estrogen: evidence for a steroid receptor fast action complex (SRFC) in caveolae. Steroids67(6), 413-419.
3. Cunninghum., Leveno., Bloom., Hauth., Rouse., and Spong. (2010). Williams Obstretrics. 23rd Ed. U.S. McGraw-Hill. P 38-43.
4. Filicori, M., Butler, J.P., and Crowley, W.F. Jr. (1984). Neuroendocrine regulation of the corpus luteum in the human. J Clin invest73,1638.
5. Giraud, G.D., Morton, M.J., and Thornburg, K.L. (1990). Ovarian secretions and cardiovascular functions. In: Ovarian Secretions and Cardiovascular and Neurological Function (eds. Naftolin, F., Gutmann, J.N., Decherney, A.H., and Sarrel, P.M.), Seronosymposia publications, Raven Press, New York. P 93-125.
6. Girdler, S.S., Pedersen, C.A., Stern, R.A., and Light, K.C. (1993). Menstrual cycle and premenstrual syndrome: modifiers of cardiovascular reactivity in women. Health Psychol12, 180-192.
7. Girija, B., and Veeraiah, S. (2011). Effects of different phases of menstrual cycle on physical working capacity of an Indian population. Indian J Physiol Pharmacol55(2), 165-169.
8. Hassan, A.A.K., Carter, G., and Tooke, J.E. (1990). Postural vasoconstriction in women during the normal menstrual cycle. Clin Sci78, 39-47.

9. Hernandez, I., Delgado, J.L., Diaz, J., Quesada, T., Teruel, M.J., and Lianos, M.C., et al. (2000). 17-beta-estradiol prevents oxidative stress and decreases blood pressure in ovariectomized rats. Am J Physiol Regul Integr Comp Physiol279R, 1559-1605.
10. Hoff, J.D., Quigley, M.E., and Yen, S.C.C. (1983). Hormonal dynamics at midcycle: A re-evaluation. J Clin Endocrinol Metab57, 792.
11. Kaplan, B.J., Whitsett, S.F., and Robinson, J.W. (1990). Menstrual cycle phase is a potential confound in psychophysiology research. Psychophysiology27, 445-450.
12. Kellehar, C., Joyce, C., Kelly, G., and Ferriss, J.B. (1986). Blood pressure alters during the normal menstrual cycle. Br. J Obstet Gynaecol93, 523-526.
13. Kelleher, C., Joyce, C., Kelly, G., and Ferriss, J.B. (1986). Blood pressure alters during the normal menstrual cycle. Br. J Obstet Gynaecol93, 523-526.
14. Leathard, H.L., and Eccles, N.K. (1991). Inhibition and enhancement of human vascular contractility by ovarian steroids: candidate mechanisms linking migraine incidence with the menstrual cycle. In: New Advances in Headache Research: 2(ed. Rose, E.F.), Smith-Gordon, London.
15. Manhem, K., and Jern, S. (1994). Influence of daily-life activation on pulse rate and blood pressure changes during the menstrual cycle. J Hum Hypertens8, 851-856.
16. McKinley, P.S., King, A.R., Shapiro, P.A., Slavov, I., Fang, Y., and Chen, I.S., et al. (2009). The impact of menstrual cycle phase on cardiac autonomic regulation. Psychophysiology46(4), 904-911.
17. Reed, B.G., and Carr B.R., (Updated 2018 Aug 5). The normal menstrual cycle and the control of ovulation. In: Fiengold, K.R., Anawalt, B., Blackman, M.R., et al., editors. Endotext (internet). South Dartmouth (MA): MDText.com., Inc.: 2000-. https://www.ncbi.nlm.nih.gov/books/NBK279054/
18. Sato, N., Miyake, S., Akatsu, J., and Kumashiro, M. (1995). Power spectral analysis of heart rate variability in healthy young women during the normal menstrual cycle. Psychosomatic Medicine57, 331-335.
19. Tousignant-Laflamme, Y., and Marchand, S. (2009). Autonomic reactivity to pain throughout the menstrual cycle in healthy women. Clinical autonomic Research19, 167-173.
20. Vallejo, M., Márquez, M.F., Borja-Aburto, V.H., Cárdenas, M., Hermosillo, A.G. (2005). Age, body mass index, and menstrual cycle influence young women's heart rate variability. Clinical Autonomic Research15, 292-298.
21. Du Xiang, Yang, L., Shujun, Z., Encheng, Z., and Yanfeng, W. (2021). Protective effects of Estrogen on cardiovascular disease mediated by oxidative stress. Oxidative Medicine and Cellular Longevity2021, Article ID 5523516, 15 pages.
22. Yazar, Ş., and Yazici, M. (2016). Impact of menstrual cycle on cardiac autonomic function assessed by heart rate variability and heart rate recovery. Med Princ Pract25, 374-377.
23. Yildirir, A., Kabakci, G., Akgul, E., Tokgozoglu, L., and Oto, A. (2002). Effects of menstrual cycle on cardiac autonomic innervations as assessed by heart rate variability. Annals of Noninvasive Electrocardiology7, 60-63.