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**Physiology**

# Assessment of Heart Rate Variability between Premenopausal and Postmenopausal Women

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| Abstract | | Original Research Article |

Menopause causes an imbalance of the autonomic nervous control of cardiovascular system.Therefore it's associated with decreased heart rate variability (HRV), which is due to reduced parasympathetic or increased sympathetic outflow to the heart. The objective of our study was to compare HRV between premenopausal and postmenopausal women. Anthropometric measurements such as age, height, weight, BMI were measured. A total of 60 normotensive both married as well as unmarried females (30 premenopausal and 30 postmenopausal) were included. HRV was recorded and the data were subjected to time domain and frequency domain analysis. In frequency domain parameters we observed that parasympathetic activity predominates as indicated by Total Power (ms²), HF (ms$^2$) in premenopausal women as compared with postmenopausal group although the difference was not significant. In time domain parameters, we found a significant difference in mean HR between two groups. The comparative decrease in HRV in postmenopausal women implies a considerable reduction in autonomic modulation, which can be attributed to change in hormonal factors.
**Keywords:** Premenopausal, postmenopausal, HRV, sympathetic activity, parasympathetic activity.

## INTRODUCTION

Menopause is defined as the time of cessation of ovarian function resulting in permanent amenorrhea. It takes 12 months of amenorrhea to confirm that menopause has set in therefore it is a retrospective diagnosis [1].

Menopause is multidimentional and influenced by many endogenous and exogenous factors mainly perceived as reproductive hormones deficiency. Their deficiency affects much metabolic and physiological function in the women's body including cardiovascular system. Postmenopausal women have increased risk of metabolic syndrome including dyslipidemia, insulin resistance, hypertension and cardiovascular disease [2].

Menopause causes an imbalance of the autonomic nervous control. 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 noninvasive tool, can assess the balance between sympathetic and parasympathetic regulation on cardiac activity. Increased regularity of heart beat activity corresponds to decreased HRV and vice- versa. Decreased HRV reflects the increased sympathetic tone or decreased parasympathetic activity and is considered an important cardiovascular risk factor [3].

Various studies have shown that parasympathetic activity is predominant among premenopausal women and sympathetic activity is predominant among postmenopausal women through only frequency domain analysis of HRV. Moreover, only few studies have been conducted on Indian population.

Therefore, present study is aimed to compare time domain as well as frequency domain analysis of HRV between premenopausal and postmenopausal women.

## MATERIALS AND METHODS

This observational study was conducted in the research lab of department of physiology after the

approval from institutional ethical committee on human experimentation and with the Helsinki declaration of 1975 revised in 2000. Informed consent was obtained from the subjects before the start of study. A total of 60 apparently healthy normotensive both married as well as unmarried 30 premenopausal women and 30 postmenopausal women were included. Purposive sampling technique was used. All subjects underwent short-term lead II ECG recording to obtain HRV, during the same hours of the day (9am- 12pm) to avoid confounding, effect of circadian rhythm on autonomic activity. In premenopausal women, HRV was recorded during follicular phase of menstrual cycle. All the participants were advised to refrain from eating and drinking (water, tea and coffee) 2 hours before presenting themselves to the lab.

**The subjects were divided in two groups**
Group I consisting of 30 premenopausal women.
Group II consisting of 30 postmenopausal women

# INCLUSION CRITERIA
Eumenorrheic premenopausal women aged between 18-42 years having regular 28-32 days menstrual cycle for at least for last 6 months prior to the study were recruited. Postmenopausal women aged 43-55 years, with or without symptoms, were all included. All the postmenopausal women in the study reported that they had menopause naturally at least one year before.

# EXCLUSION CRITERIA
In both groups, smokers, alcoholics and subjects taking any drug affecting ANS or suffering from any endocrine disease, cardiorespiratory disease, any psychiatric illness were excluded. Postmenopausal women who had hysterectomy or oophorectomy done or had undergone Hormone Replacement Therapy (HRT) were excluded as well.

**Anthropometric measurements**
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/m² was calculated by Quetelet's index.

**Recording of HRV**
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 [4]. 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 4.0.2 (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), NN50 (% of number of instances in which two consecutive NN intervals differ by more than 50msec) and different frequency domain indices such as total power (TP) in absolute values (ms2), low frequency (LF) component (0.04–0.15 Hz), high frequency (HF) component (0.15–0.4 Hz) in absolute (ms2) and normalized units (nu) and LF-HF ratio were recorded.

# STATISTICAL ANALYSIS
Statistical package for the social sciences (SPSS) version 19 software for windows and Microsoft excel were used for statistical analysis. All values were expressed as mean±SD. Unpaired t test was applied. Values were considered significant for $p < 0.05$ with a confidence interval of 95%.

# RESULT
Table 1 shows anthropometric measurements between premenopausal women (n=30) and postmenopausal women (n=30). There was significant difference (P = 00) in age, height, weight and BMI between the two groups. Table 2 shows the frequency variables in HRV between the premenopausal women and postmenopausal women. All the frequency domain variables except HF (nu) were higher in premenopausal women, although we did not find any significant difference (P > 0.05) between the two groups.

Table 3 shows time domain variables in HRV between premenopausal and postmenopausal women. The mean HR (bpm) was significantly lower (P value = 0.038) in premenopausal women (81.1 ± 13.10) than in postmenopausal women (87.83 ± 11.34) while SDNN (ms²), RMSSD, NN50, mean RR (s) were insignificantly higher (P > 0.05) in premenopausal women than postmenopausal women.

**Table-1: Anthropometric Measurements in premenopausal and postmenopausal women (n=30, in each group)**

| | PREMENOPAUSAL WOMEN (mean ± SD) | POSTMENOPAUSAL WOMEN (mean ± SD) | P value |
|---|---|---|---|
| AGE (Yrs) | 29.13±8.03 | 51.7±4.05 | *00 |
| HEIGHT (cms) | 157.46±2.09 | 154.83±3.06 | *00 |
| WEIGHT (kgs) | 60.56±3.54 | 68.6±3.6 | *00 |
| BMI (kg/m$^2$) | 24.46±1.43 | 28.62±1.12 | *00 |

*statistically significant (P<0.05)

**Table-2: Frequency Variables of HRV in premenopausal and postmenopausal women (n=30, in each group)**

| HRV variables | PREMENOPAUSAL WOMEN (mean ± SD) | POSTMENOPAUSAL WOMEN (mean ± SD) | P value |
|---|---|---|---|
| TP(ms²) | 676.88 ± 704.75 | 499.56 ± 564.15 | 0.287 |
| LF(ms²) | 179.80 ± 226.42 | 120.06 ± 167.27 | 0.25 |
| LF(n.u.) | 51.30 ± 19.86 | 49.12 ± 17.26 | 0.651 |
| HF(ms²) | 161.63 ± 211.10 | 145.31 ± 228.42 | 0.775 |
| HF(n.u.) | 48.69 ± 19.86 | 49.21 ± 17.56 | 0.915 |
| LF/HF | 1.48 ± 1.14 | 1.29 ± 1.05 | 0.509 |

**Table-3: Time Domain variables of HRV in premenopausal and postmenopausal women (n=30, in each group)**

| HRV variables | PREMENOPAUSAL WOMEN (mean ± SD) | POSTMENOPAUSAL WOMEN (mean ± SD) | P value |
|---|---|---|---|
| SDNN(ms²) | 38.47 ± 19.09 | 31.61 ± 12.00 | 0.101 |
| RMSSD | 31.01 ± 15.72 | 27.43 ± 14.91 | 0.37 |
| NN50 | 57.4 ± 57.06 | 36.16 ± 45.20 | 0.116 |
| mean RR(s) | 0.96 ± 1.51 | 0.76 ± 0.13 | 0.461 |
| mean HR(bpm) | 81.1 ± 13.10 | 87.83 ± 11.34 | *0.038 |

*statistically significant (P<0.05)

# DISCUSSION

Our data indicate a decrease in HRV, to be an expression of a reduction in autonomic modulation in postmenopausal women compared to premenopausal women, which most likely was due to the decrease in parasympathetic modulation in sinus node. This decrease can possibly be associated with hormonal factors, primarily due to decreased estrogen hormone due to inactivity of graffian follicles (ovaries).

Our results are in coherence with prior studies and reveals that parasympathetic activity is predominant among premenopausal women & sympathetic activity is predominant among postmenopausal women.

In anthropometric measurements we found significant values, which itself implied that Menopause was also accompanied by reduced energy expenditure, both during rest and physical activity. An accelerated loss of fat-free mass, alteration of adipose tissue metabolism and fat oxidation also occur. This deregulation of energy metabolism could induce an increase in total adiposity and a redistribution of fat in the abdominal region in Postmenopausal women.

In a study, Matthews *et al*. concluded that the menopausal transition affects body mass index in mid-life, but the effect is small relative to other influences [5].

In our study, we observed that TP (P=0.287) and HF (P=0.775), though not significant, but were comparatively higher in Premenopausal women than that in postmenopausal women. Thus, suggesting parasympathetic dominance in premenopausal women and sympathetic dominance in postmenopausal women.

Whereas, time domain variables show overall magnitude of HRV. Mean HR was significantly higher (P=0.038) in postmenopausal women due to sympathetic dominance. While SDNN (P=0.101), RMSSD (P=0.37), NN50 (P=0.116), mean RR (P=0.461) were higher in premenopausal women as compared to postmenopausal women, due to parasympathetic dominance.

In a study, Natrajan *et al*. found that TP (P=0.003), an index of parasympathetic activity, was significantly higher among premenopausal women, whereas LF (nu), HF (nu) and LF/HF ratio were similar among both the groups [6].

In a study Yang *et al*. concluded that sympathetic activity, as indicated by LF/HF ratio, was lower among postmenopausal women treated with estrogen only compared to postmenopausal women treated with combination of estrogen and progesterone. They observed a higher vagal modulation of heart rate that seems typical for younger women becomes after menopause similar to that of men. They also observed a positive shift of HRV parameters toward more beneficial values as for a cardiovascular risk in postmenopausal women treated with estrogens but not in those treated by combined estrogen - progesterone substitution therapy [7].

Tanu *et al*. studied the effect of estrogen level and body fat composition on HRV between pre and postmenopausal women from health care professional. It was found that, in postmenopausal women, LF and LF/HF were significantly higher (P<0.001), while TP and HF were significantly lower (P>0.001) [8].

Moodithaya SS *et al*. found evidences regarding the extent to which age-related changes in HRV depend on changes in levels of estrogen and body composition as it occurs from premenopausal state to postmenopausal state. They observed that postmenopausal women had significantly lower HF (P < 0.01) and higher LF (P < 0.01). The ratio of LF/HF, the index of sympathovagal balance was significantly higher (P < 0.01) among postmenopausal women. They concluded that age was one of the important confounder, responsible for the differences in all the components of power spectrum between the two study groups [9].

Ribeiro *et al*. studied HRV under resting conditions in postmenopausal and young women. They concluded a decrease in parasympathetic modulation in postmenopausal women compared to young women which was possibly due both to the influence of age and hormonal factors [10].

It is hypothesized that endogenous estrogen contributes to parasympathetic predominance in premenopausal women. Estrogen increases cholinergic activity at central & peripheral levels, which suppresses sympathetic tone and elevates parasympathetic tone. It has been found that estrogen receptors in hypothalamic neurons & hypothalamus are the centre for autonomic nervous system. Thus, estrogen modulates autonomic activity by acting through these neurons. In addition, the presence of estrogen receptors in the heart, vascular smooth muscle & autonomic brainstem centres (eg. Nucleus tractus solitarius, ventrolateral medulla) suggests the involvement in regulation of cardiovascular system [11].

As life expectancy increases, women in general experience a longer life after menopause and increased health hazards. The altered sympathovagal activity has an additional adverse effect on health profile and ultimately, on the quality of life, of Postmenopausal women. Dietary modifications, exercise, yoga, acupressure therapy and medications may improve autonomic functions in Postmenopausal women [12].

Our study has limitations. Sample size was small in both groups. Also, we have not recorded HRV with 24 hours holter monitoring which is a better choice to measure HRV. Further, the study can be expanded by correlating hormonal assay (estrogen and progesterone), Autonomic function tests, and Lipid profile. Postmenopausal women were not divided according to menopausal symptoms.

# CONCLUSION

Based on the above study we concluded that the comparative decrease in HRV in postmenopausal women implies a considerable reduction in autonomic modulation, which can be attributed to change in hormonal factors. Our study showed that parasympathetic activity predominates as indicated by TP (ms²), HF (ms²) in premenopausal women in comparison to postmenopausal women. In time domain parameters, we found a significant difference in mean HR between two groups. BMI of postmenopausal women were significantly higher than control subjects, suggestive of sympathetic dominance. Interventions to increase physical activity are highly recommended to prevent increases in adiposity common in mid-life.

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