



## COMPARISON OF CARDIAC AUTONOMIC ACTIVITY IN PRE- AND POST-MENOPAUSAL WOMEN USING HEART RATE VARIABILITY

**Ms. Divya Harsh**

Ph.D. Scholar, Department of Physiology, Dr. Sampurnanand Medical College, Jodhpur, Raj

**Dr. Raghuvver Choudhary\***

Sr. Professor & Head of the Department, Department of Physiology, Dr. SNMC, Jodhpur, Raj. \*Corresponding Author

**Dr. Kamla Choudhary**

Associate Professor, Department of Physiology, Dr. SNMC, jodhpur

**ABSTRACT** **Background** - Heart Rate Variability (HRV) has been considered as the most sensitive measure of autonomic function when evaluating sympathovagal balance. It has also been suggested that the effects of estrogen cause parasympathetic dominance in women of reproductive age and sympathetic hyperactivity in postmenopausal women. **Aim and Objectives** – The aim of the study was to compare the basal cardiovascular parameters and HRV between premenopausal and postmenopausal women. **Material and Methods** – This was a cross-sectional observational study carried out in Dr. Sampurnanand Medical College, Jodhpur, Rajasthan. After 15 min of rest, HRV was recorded among 40 premenopausal and 40 postmenopausal women in the supine position for 5 min using AD Instruments, Australia. The frequency domain parameters of HRV were analyzed Heart Rate Variability was assessed by “C Series HRV System – Lab-Chart 8 (MLS310/8, Windows or Mac), ADINSTRUMENTS, Australia. The data were presented as mean (SD). Student's Independent t-test was used to find the statistical difference between the two groups. p-Value < 0.05 was considered statistically significant. **Results** - Systolic blood pressure (p = 0.00), pulse pressure (p = 0.00), and HbA1c% (p = 0.00) values were significantly higher in postmenopausal women compared to premenopausal women. HF (nu), an index of parasympathetic activity, was higher among premenopausal women. LF (nu), and LF/HF ratio were higher among both the groups. **Conclusion** – Our study revealed no significant changes in LF (nu), HF (nu), or the LF/HF ratio between the two groups. However, overall pre-menopausal women exhibit higher parasympathetic activity. These findings are may be the result of influence of estrogen, which is greater in premenopausal women than in postmenopausal women,

**KEYWORDS** : Menopause, Heart Rate Variability, Frequency Domain Measures.

### INTRODUCTION –

Menopause is a natural cessation of menstruation i.e. ovaries stop producing estrogen and progesterone. Decreased concentration of these hormones impacts several organ systems, including cardiovascular system. Heart is an organ under the influence of autonomic nervous activities, thereby maintaining its rate on the beat-to-beat variation. Also, it should emphasize that variability of heart rate can be measured by a non-invasive method with the least error using cheaper and simple equipment.

Heart Rate Variability (HRV) is the beat-to-beat variation (variation in cardiac cycle length) of the heart, a phenomenon, that occurs mainly due to cardiac activity during the respiratory cycle (respiratory sinus arrhythmia) at rest. HRV is dependent on Sino-atrial node for the rate of discharge which is under the control of parasympathetic nervous system and respiratory sinus arrhythmia because of variation in vagal tone during inspiration and expiration. Therefore, being influenced by both the sympathetic and parasympathetic, HRV becomes the most useful way of assessing the sympathovagal balance. There are two parts to the HRV power spectrum. They are divided into low frequency (LH) and high frequency (HF) components. The parasympathetic component is represented by the HF component, while the sympathetic component is represented by the LF component. Symathovagal balance is reflected in the LF/HF ratio. Menopause induces a shift toward sympathetic hyperactivity in the autonomic nervous system's regulation of the cardiovascular system.<sup>1</sup> Compared to the premenopausal group, the postmenopausal group's vagal and sympathetic activity were, respectively, lower and greater. Furthermore, postmenopausal women receiving conjugated estrogen replacement treatment had much higher vagal and lower sympathetic heart rate modulations.<sup>2</sup> Compared to premenopausal women, postmenopausal women had a change in their autonomic state, with a greater sympathetic and a lower vagal tone.<sup>3</sup> Women who had gone through menopause but weren't on hormone replacement treatment (HRT) showed elevated sympathetic tone.<sup>4</sup> According to epidemiological research, women experience a lower incidence of cardiovascular illness than men do, however this difference disappears after menopause.

Fewer research has been done in the Indian population, despite the fact that several Western studies have demonstrated that postmenopausal

women exhibit sympathetic hyperactivity when compared to premenopausal women. Therefore, the current study's goal was to compare HRV in Indian population premenopausal and postmenopausal women.

### MATERIAL AND METHODS –

This study was a cross-sectional observational study, carried out at Dr. Sampurnanand Medical College, Jodhpur, Rajasthan, after obtaining approval from Institutional Ethics Committee. The study population was divided into two groups, one is control group consists of 40 premenopausal group and 40 post-menopausal women under study group aged >45 years to <65 years. Written informed consent of females was collected.

Inclusion Criteria	Exclusion Criteria
Pre-menopausal women 1. Apparently healthy (showing no signs of illness) non-athletic females. 2. Women with regular menstrual cycle – average cycle is 28 days long, anything between 21 - 45 days is considered normal. The time from the first sign of blood to the last is usually in the 3-to-5-day range. Any length from 2 days to a week is normal for a period.	1. Metabolic Syndrome. 2. Pregnant, lactating women. 3. History of exogenous estrogen or tamoxifen therapy since last year. 4. A history of induced menopause due to bilateral oophorectomy, radiation, or drug use. 5. A history of ischemic heart disease, stroke, or thyroid or hepatobiliary disease. 6. Alcoholic/ smokers 7. Menorrhagia/ Menorrhagia 8. Use of any antipsychotic drug, antiepileptic drug and Herbal drugs. 9. Subjects on Weight reduction medications in last month.
Postmenopausal women 1. At least twelve consecutive months of amenorrhea <sup>32</sup> . (Amenorrhea is physiological during pregnancy, lactation, prior to puberty and after menopause.)	

Anthropometric measurements (weight, height, waist circumference,

hip circumference, waist-to-hip ratio, BMI and biochemical tests), cardiovascular parameters (blood pressure, resting heart rate) were recorded. HRV was recorded in supine position in our Departmental research laboratory in the pre-noon timings using ADINSTRUMENTS, Australia. Heart Rate Variability was assessed by "C Series HRV System – Lab-Chart 8 (MLS310/8, Windows or Mac), ADINSTRUMENTS, Australia. The spectral HRV indices were evaluated which included frequency domain measures – normalized low-frequency power (LFnu), normalized high-frequency power (HFnu), and ratio of low-frequency power to high-frequency power (LF/HF ratio). HFnu are measures of parasympathetic activity and LFnu and LF/HF ratio are measures of the sympathetic activity.

#### STATISTICAL ANALYSIS -

The data are presented as mean (SD). Analysis was done by using SPSS version 22. Independent student t-test was used for statistical difference between the two groups. p-value (<0.05) was considered statistically significant.

#### RESULTS

Table 1 shows body mass index (BMI) and basal cardiac parameters of the pre- and post-menopausal groups. It was observed that the BMI was comparable between the two groups. It was seen that the systolic blood pressure ( $p < 0.01$ ) and pulse pressure ( $p < 0.01$ ) were significantly higher in postmenopausal women compared to premenopausal women. Other parameters were within normal limits in both the groups. Body Mass Index, diastolic blood pressure, and men arterial pressure showed similar values in both the groups.

Table 2 shows the frequency domain measures of HRV of two groups. In HRV, lower HF, an indicative of parasympathetic activity and higher LF and LF/HF ratio, representing sympathetic activity in postmenopausal women.

**Table 1** BMI and basal cardiovascular parameters of premenopausal women and postmenopausal women, expressed as mean (SD)

Parameters	Premenopausal Group	Postmenopausal group	p-value
Age	47.60 ± 2.64	55.68 ± 5.09	0.00
BMI (Kg/m <sup>2</sup> )	31.56 ± 16.43	140.15 ± 24.87	0.56
Systolic BP (mmHg)	124.10 ± 16.85	140.15 ± 25.87	0.00
Diastolic BP (mmHg)	79.80 ± 10.62	81.55 ± 13.90	0.52
Pulse Pressure (mmHg)	44.38 ± 10.62	58.62 ± 15.84	0.00
MAP (mmHg)	93.55 ± 12.19	99.15 ± 17.02	0.09
Heart Rate (beats/min)	78.84 ± 11.60	78.82 ± 12.73	0.99
HbA1c%	5.45 ± 0.49	5.69 ± 0.48	0.00

BMI – Body Mass Index, MAP- Mean Arterial Pressure

Statistically analysis was done by Student's Independent t test, p-value < 0.05 was considered statistically significant.

**Table 2** Frequency domain indices of HRV in premenopausal and postmenopausal women, expressed as mean (SD)

Parameters	Premenopausal Group	Postmenopausal Group	p-value
LFnu (ms <sup>2</sup> )	56.71 ± 20.79	57.36 ± 20.64	0.61 NS
HFnu (ms <sup>2</sup> )	44.12 ± 19.65	43.59 ± 17.61	0.90 NS
LF/HF ratio	1.81 ± 1.47	1.88 ± 1.90	0.86 NS

LFnu (ms<sup>2</sup>), Low Frequency expressed in normalized units; HFnu (ms<sup>2</sup>) High- frequency expressed in normalized units.

Statistically analysis was done by Student's Independent t-test, p-value > 0.05 was considered statistically non-significant.

#### DISCUSSION

Heart Rate Variability is an emergent property of interdependent regulatory systems which operate on different time scales which help us adapt to environmental and psychological challenges. It reflects regulation of autonomic balance, blood pressure (BP), gas exchange, gut, heart and vascular tone which shows to the diameter of the blood

vessels that regulate blood pressure.<sup>5</sup> In the present study, on comparison of HRV parameters in pre-menopausal and post-menopausal women, we observed decrease in mean values of HF (nu) while lower mean values of LF (nu) and LF/HF ratio in post-menopausal women, although we are unable to find significant differences between both the groups. Our results are concordant to the results of Natarajan et al. (2015).<sup>6</sup> Lower vagal tone, greater sympathetic tone, and a correlation with more lethal ventricular arrhythmias are all indicated by reduced HRV. Therefore, these modifications point to a disturbance of the autonomic nervous system.<sup>7</sup>

Although we were unable to establish sympathetic hyperactivity in postmenopausal women, our work has demonstrated that parasympathetic activity is prominent in premenopausal women. Endogenous estrogen is thought to have a role in premenopausal women's parasympathetic dominance. Estrogen reduces sympathetic tone and raises parasympathetic tone via increasing cholinergic activity at the central and peripheral levels. It is already known that the hypothalamus is the center for autonomic nervous system and has estrogen receptors in it. So, through these neurons, estrogen regulates autonomic activity. Furthermore, the participation in the control of the cardiovascular system is suggested by the presence of estrogen receptors in the heart, vascular smooth muscle, and autonomic brainstem regions (such as the ventrolateral medulla and nucleus tractus solitarius).<sup>3</sup> Rosano et al.'s study<sup>9</sup> revealed that postmenopausal women's main sympathetic activity declined following a four-month course of estrogen replacement medication. When analyzing time domain HRV data, Ribeiro et al.<sup>10</sup> found that postmenopausal women had lower HRV (a drop-in parasympathetic activity) than pre-menopausal female. According to Yang et al.<sup>11</sup> postmenopausal women treated with estrogen alone had reduced sympathetic activity as measured by the LF/HF ratio in comparison to postmenopausal women treated with a combination of estrogen and progesterone. It was also demonstrated by Sorensen<sup>12</sup> that estrogen provided postmenopausal women with cardiovascular protection. The follicular phase of the menstrual cycle, when estrogen levels were higher, was when parasympathetic activity predominated, as demonstrated by Saeki et al.<sup>13</sup> In contrast to postmenopausal women without estrogen therapy, Stampfer et al.'s research<sup>14</sup> found that postmenopausal women receiving estrogen replacement therapy had a decreased risk of cardiovascular disease. Thus, using HRV analysis, several studies have demonstrated that parasympathetic activity is prevalent in premenopausal women whereas sympathetic activity is predominated in postmenopausal women. The existence or lack of estrogen has been linked to these consequences.

Therefore, it is possible that estrogen is the cause of the premenopausal women increased parasympathetic activity in our research. However, we are unable to demonstrate the impact of low estrogen levels in postmenopausal women. The smaller sample size in our study is one of its limitations.

#### CONCLUSION

In premenopausal women, estrogen may be linked to higher parasympathetic activity. This might be the cause of estrogen's cardioprotective effects in women who are not yet menopausal. HRV is a screening test that may be used to identify postmenopausal women who need hormone replacement therapy (HRT) by detecting autonomic dysfunction in these individuals.

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