

## Sympathetic Nerve Function Status in Postmenopausal Women

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### Abstract

**Background:** Postmenopausal women usually suffer from increased incidence of cardiovascular diseases than premenopausal women. Alterations in autonomic nerve functions often develop in this group of women that commonly affect cardiac vagal control and usually associated with sympathetic hyperactivity. **Objectives:** To observe the sympathetic nerve function status in postmenopausal women and their relationships with serum estrogen level. **Methods:** This cross sectional study was carried out in the Department of Physiology, BSMMU, Dhaka from 1<sup>st</sup> January to 31<sup>st</sup> December 2007. A total number of 60 apparently healthy subjects of whom 30 were postmenopausal women with age ranged from 45-60 years (group B) and 30 were premenopausal women with age ranged from 20-30 years (group A) were enrolled. Premenopausal women were studied during follicular phase of menstrual cycle. Two simple autonomic nerve function tests, rise of diastolic blood pressure (DBP) during hand grip and fall of systolic blood pressure (SBP) on standing were done to assess sympathetic activity and serum estrogen level was measured in both the groups. Data were analysed by unpaired t test and Pearson correlation coefficient test. **Results:** Mean resting SBP and DBP were significantly higher ( $p < 0.001$ ) in postmenopausal women than premenopausal women. The mean value of estrogen was significantly ( $p < 0.001$ ) lower in group B (postmenopause) than those in group A (premenopause). Fall in systolic blood pressure after standing was significantly ( $p < 0.001$ ) higher and rise in diastolic blood pressure after sustained handgrip was significantly ( $p < 0.001$ ) lower in postmenopausal women than those in premenopausal women during their follicular phase of menstrual cycle. Again, rise in diastolic blood pressure after sustained handgrip and fall in systolic blood pressure after standing showed ( $p > 0.05$ ) negative correlation with estrogen level in the postmenopausal women which was statistically not significant. In addition, regression analysis further revealed significant association of sympathetic activity with estrogen level and age in postmenopausal women. **Conclusion:** From this study it can be concluded that sympathetic activity is higher in postmenopausal women, which may be related to their low estrogen level and age as well.

**Key words:** Postmenopause, sympathetic nerve functions, estrogen.

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**M**enopause is a non-reproductive phase of life in women, where the production of ovarian hormones gradually decreases<sup>1,2</sup>. Alterations in autonomic nerve

functions often develop in this group of women that commonly affect cardiac vagal control and usually associated with sympathetic hyperactivity<sup>3</sup>. This alteration of autonomic functions may cause structural and functional

changes at the myocardium and large arteries, which consequently directed towards the development of hypertension<sup>4,5</sup>. It may also promote cardiac arrhythmias, which induces left ventricular hypertrophy and reduces the compliance of the large arteries<sup>5</sup>. Moreover, increased sympathetic activity may lead to sudden cardiac death<sup>6</sup>. So, menopausal women may gradually be hypertensive with increased heart rate due to autonomic nerve dysfunction<sup>3</sup>.

In early 1970s Ewing et al. have considered five simple non invasive cardiovascular reflex tests to evaluate the status of cardiovascular autonomic control<sup>7</sup>. Among them fall of systolic blood pressure(SBP) after sudden standing (orthostatic test) and rise of diastolic blood pressure(DBP) during sustained handgrip are the 2 indices of sympathetic nerve function<sup>8</sup>.

In an investigation on sympathetic nerve function status in postmenopausal women Bhat et al. found that fall in systolic blood pressure after standing and rise in diastolic blood pressure during sustained handgrip, have increased significantly in respect to normal established range<sup>9</sup>.

A large number of postmenopausal women our country are at the risk of developing postmenopausal complication including cardiovascular diseases associated with autonomic nerve dysfunctions. Recent attention on postmenopausal health has led several countries to study autonomic nerve function status in postmenopausal women and they have demonstrated the relationships of decreased level of estrogen with autonomic nerve dysfunction<sup>3,6,9-11</sup>. However, no such investigation was reported in our country. Therefore, the present study was done to observe the sympathetic nerve function status, one component of autonomic nerve function in healthy Bangladeshi postmenopausal women. It is expected that the out come of the study may help to identify the silent presence of impaired sympathetic nerve function in postmenopausal population and thereby help the physicians to

take appropriate measure for prevention of complications.

### Methods

The present cross sectional study was carried out in the Department of physiology, BSMMU, Dhaka from January to December 2007. In this study a total number of 60 apparently healthy subjects were selected, of whom 30 were postmenopausal with age ranged from 45 to 60 years and 30 were premenopause with age ranged from 20 to 30 years. The duration of the natural and surgical menopause was at least one year and they were not under any form of HRT. Premenopausal women were studied during follicular phase of menstrual cycle. Protocol of this study was approved by the Ethical committee of the Department of Physiology. The aim and objectives of the study was explained to each of the subject in details and then written informed consent was taken. A thorough clinical examination of all subjects were done. Height and weight of each subject was measured and BMI was calculated. Under aseptic precaution 5 ml of blood was collected and serum was prepared for estimation of estrogen level. Sympathetic nerve function of each of the subjects was evaluated by two cardiovascular reflex test. Orthostatic test estimates systolic blood pressure response after sudden standing from lying position and handgrip test measures diastolic blood pressure response to sustained hand grip. Serum estrogen level of each subject was measured by AxSYM method<sup>12</sup>.

Data were analyzed by unpaired student t test, Pearson's correlation coefficient test and multiple regression analysis as applicable. The statistical analysis was done by SPSS program version-11.5.

### Results

Demographic data of the subjects are presented in the Table I.

The mean estrogen level was significantly ( $p < 0.001$ ) lower in group B than those in group A (Figure 1) Resting heart rate was comparable

between the groups. But resting systolic and diastolic blood pressures were significantly higher ( $p < 0.001$ ) in postmenopausal women than those in premenopausal women (Table II). Fall in systolic blood pressure after standing was significantly ( $p < 0.001$ ) higher and rise in diastolic blood pressure after sustained handgrip was significantly ( $p < 0.001$ ) lower in postmenopausal women compared to premenopausal women during their follicular phase (Figure 2 & 3).

Again, with serum estrogen level, fall in systolic blood pressure and rise in diastolic blood pressure were negatively correlated in postmenopausal women though all these correlations were statistically non significant (Figure 4&5). Furthermore, Regression analysis revealed significant association of rise in diastolic blood pressure with age in postmenopausal women. (Table III)

**Table I:** Age and BMI in different groups (n=60)

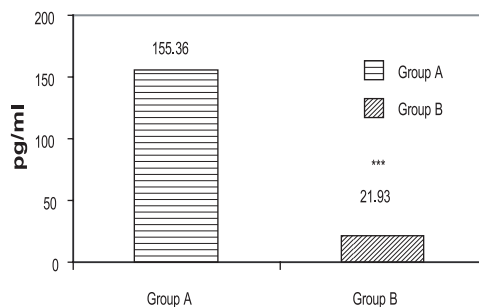
Variables	A (n=30)	B (n=30)
Age (years)	24.30±3.88	50.53±3.02
BMI (kg/m <sup>2</sup> )	20.80±1.40	22.18±3.08

Data are expressed as mean ±SD.

A = Premenopause in follicular phase (control group)

B = Postmenopause (study group)

n = Total number of subjects



Group A = Premenopause in follicular phase (control)  
Group B = Postmenopausal (study)

**Figure 1:** Mean Serum Estrogen Levels in Different Groups (n=60)

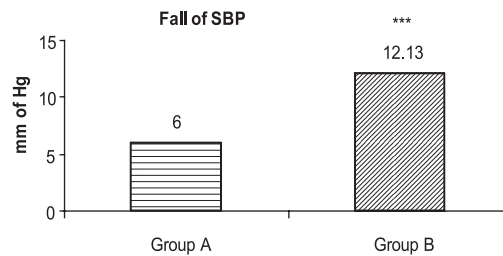
**Table II:** Resting Heart Rate and Blood Pressures In Different Groups (n=60)

Groups	Heart rate (beats/min)	Blood pressure (mm of Hg)	
		SBP	DBP
A (n=30)	77.26±6.73	100.16±5.79	67.66±6.26
B (n=30)	77.80±7.37 <sup>ns</sup>	116.66±14.34*	75.66±6.78*

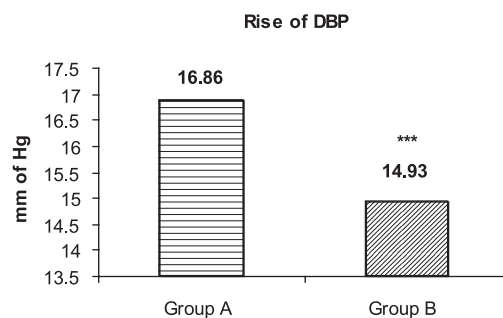
Statistical analysis done by un paired t test

Data are shown as mean± SD.

\*= $p < 0.001$ , ns= not significant, n= Total number of subjects

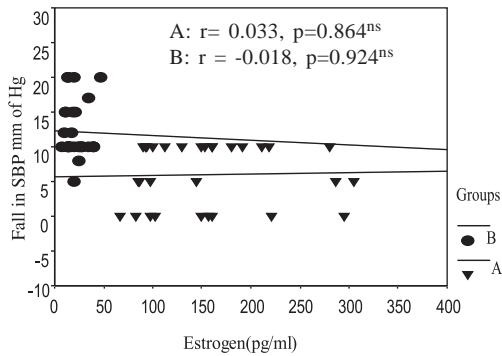


**Figure 2:** Blood pressure response to standing (fall in SBP) in different groups (n= 60)



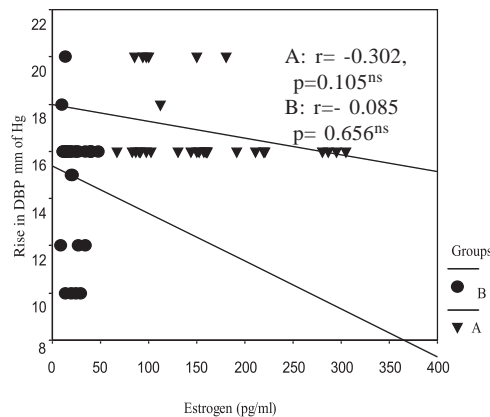
\*\*\* = $p < 0.001$

**Figure 3:** Blood pressure response to sustained handgrip (rise in DBP) in different groups (n=60)



ns =not significant

**Figure 4:** Correlation of fall in systolic blood pressure with serum estrogen level in different groups (n=60)



ns =non significant

**Figure 5:** Correlations of rise in diastolic blood pressure with estrogen level in different groups (n=60)

**Table III:** Multivariate relations between rise in diastolic BP on sustained handgrip and serum estrogen, age and BMI in postmenopausal subjects(n=30)<sup>18</sup>

Independent Variables	Dependant Variables	$\beta$ / p value
Serum estrogen	Rise in DBP during sustained handgrip	0.016 / 0.932 <sup>ns</sup>
Age		-0.375 / 0.047*
BMI		0.238 / 0.193 <sup>ns</sup>

\*= p<0.05

ns=non significant

**Discussion**

In the present study, the observed significantly lower estrogen level in post menopausal is similar to the observations made by other researchers<sup>13</sup> Again significantly higher resting systolic and diastolic blood pressures in postmenopausal women is consistent to those found by Neves et al<sup>11</sup> and Scuteri et al<sup>14</sup>.

Significantly higher fall in systolic blood pressure after standing from lying position and significantly lower rise in diastolic blood pressure during sustained handgrip indicate sympathetic hyperactivity in postmenopausal women in comparison to premenopausal women. Similar results were observed by Rosano et al. and Mercuro et al.<sup>3,10</sup> Again, Neves et al. also made similar observation but they have used spectral analysis of HRV<sup>11</sup>.

Negative correlations of fall in systolic blood pressure and rise in diastolic blood pressure with serum estrogen level in postmenopausal women is similar to those reported by<sup>11</sup>Neves et al.

Literatures have cited several factors that might be responsible for this observed higher sympathetic activity and increased resting blood pressure in the postmenopausal women in their estrogen deficient state.

Some group of investigators suggested that estrogen increases density as well as the function of presynaptic  $\alpha_2$  adrenoreceptors, which thereby result in significant decrease of NE induced responses<sup>15</sup>. So, estrogen deficiency in postmenopausal women may lead to increased basal level of norepinephrine and its vasoconstrictor responses<sup>16</sup>. Again, estrogen also acts peripherally to increase vasodilatation by increasing the production of NO and prostacycline or by decreasing the release of Endothelin from endothelium<sup>17</sup>. Moreover, estrogen has direct effect on vascular smooth muscle to cause vasodilatation<sup>18</sup>.

Presence of estrogen receptors in cardiomyocytes indicate that it may influence cardiac contractility and regulate heart rate<sup>17</sup>.Therefore estrogen deficiency in postmenopausal women may lead to

increased vasoconstriction and increased blood pressure due to sympathetic hyperactivity<sup>10,16</sup>.

Rise in diastolic blood pressure during sustained handgrip is the consequence of heart rate dependent increase in cardiac output and peripheral vasoconstriction.<sup>19</sup> In elderly women, this less rise in diastolic blood pressure may be due to lower absolute muscle tension<sup>20</sup>, desensitization of  $\alpha$ -adrenoceptors<sup>21,22</sup> and decreased  $\beta$  adrenergic responsiveness in cardiovascular system<sup>23</sup>

Again, a greater fall in systolic blood pressure on standing in elderly person may be related to a decreased heart rate due to down regulation of  $\beta_1$  adrenergic activity<sup>22</sup>. Moreover, it has been suggested that estrogen increases LDL receptors in the liver<sup>17</sup>. So, deficiency of estrogen in postmenopausal women may cause atherosclerosis due to increased LDL cholesterol in the circulation<sup>18</sup> which may cause carotid sinus hypersensitivity thereby postural hypotension<sup>24</sup>.

### Conclusion

This study concluded that sympathetic nerve function was abnormally higher in postmenopausal women, which may be related to their age and low estrogen level.

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