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## Relationship of Sympathetic Dysfunction with Disease Duration In Female Rheumatoid Arthritis Patients

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### Abstract

**Background:** Association of increased cardiovascular morbidity and higher sympathetic activity in patients with Rheumatoid arthritis (RA) has been well recognized. **Objective:** To assess sympathetic nerve function status in Rheumatoid arthritis patients and its relationship to duration of the disease. **Methods:** This study was carried out in the dept of Physiology Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka during 2010. Sixty female RA patients aged 18-50 years with duration of disease from 1 to 10 years was selected from Rheumatology wing of Medicine OPD of BSMMU. Age and BMI matched female apparently healthy subjects were control. Sympathetic nerve function status was assessed by blood pressure response to orthostatic test and sustained hand grip isometric exercise test. In these two tests, fall in systolic blood pressure (SBP) and rise in diastolic blood pressure (DBP) respectively estimates sympathetic reactivity. For statistical analysis, unpaired students t test and pearsons correlation coefficient test was applied. **Results:** Mean values of fall of SBP was higher and rise of DBP was lower in RA patients compared to control which was statistically ( $P < 0.001$ ) significant. Again rise of DBP was negatively and fall of SBP was positively correlated with duration of the disease and the relationships were statistically highly significant ( $p < 0.01$ ). **Conclusion:** The results conclude that sympathetic reflex response was reduced in RA which was deteriorated with duration of disease.

**Key words:** RA, sympathetic reactivity, hand grip test, orthostatic test.

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### Introduction

**R**heumatoid Arthritis (RA) is a chronic disease of inflammatory origin principally affecting the peripheral joints producing pain, swelling and imposing limited mobility of the joints<sup>1</sup>. But there is evidence of its involvement in many other organ and system causing hematologic disorder, Pulmonary diseases and cardiac complications.<sup>2</sup>

Recent researches investigated the link between rheumatoid arthritis and heart health and found

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RA is associated with increased cardiac mortality and accounts for one third to one half of RA related death<sup>3-4</sup>. The autonomic nervous system plays very important role in regulating cardiovascular homeostasis and RA may cause autonomic imbalance which is not well studied as well as presented conflicting results<sup>5</sup>. Higher sympathetic activity in RA was reported by some studies<sup>5</sup> whereas others found sympathetic dysfunction in RA<sup>6</sup>. Recently, orthostatic hypotension was found in 8% of RA patients<sup>2</sup>. Though, few studies investigated autonomic function in RA<sup>5-9</sup>, the effect of duration of RA on

autonomic function was scarcely studied. This study aimed to investigate sympathetic nerve function in RA and its change with duration of disease.

### Methods

This cross sectional study was carried out in the department of Physiology of Bangabandhu Sheikh Mujib Medical University (BSMMU) during 2010. Sixty diagnosed female patients of Rheumatoid arthritis aged 18 to 50 years according to American college of Rheumatology criteria<sup>10</sup> with duration of disease from one to ten years were enrolled from the Rheumatology wing of the outpatient department of medicine of BSMMU, Dhaka. Age and BMI matched 30 apparently healthy sedentary females were control. All subjects were free from history of heart disease, hypertension, liver disease, endocrine disorder, diabetes mellitus, renal disease, psychiatric illness and drugs affecting central nervous system. The study protocol was approved by central ethical review committee of the university. The aim, benefit and procedure of the study was explained to all subjects and a written informed consent from each subject was obtained. A thorough clinical examination of all subjects were done and all information were recorded in prefixed data schedule. Resting pulse rate and blood pressure were recorded. Sympathetic nerve function of all subjects were assessed by two cardiovascular reflex test described by Ewing<sup>11</sup>, orthostatic test and handgrip isometric exercise test in the autonomic nerve function laboratory of the department of Physiology of BSMMU.

Data were expressed as mean and  $\pm$ SD and was analyzed by students unpaired t test and pearson's correlation coefficient test for statistical significance.

### Results

The mean age, BMI and SBP were almost similar but the resting pulse rate ( $p < 0.05$ ) and DBP ( $p < 0.001$ ) were significantly higher in RA patients than healthy control. (Table I). The results of sympathetic nerve function parameters are presented in Table II. The magnitude of fall of

SBP after sudden standing was higher ( $p < 0.001$ ) and rise of DBP in sustained handgrip test was lower ( $p < 0.001$ ) in RA patients which was statistically significant. On further analysis, the correlation of these two markers with duration of disease showed negative correlation for rise of DBP and positive correlation for fall of SBP with duration of RA and it was statistically highly significant ( $p < 0.001$ ) (Figure 1&2).

**Table I:** Baseline characteristics of subjects in two groups (n=90)

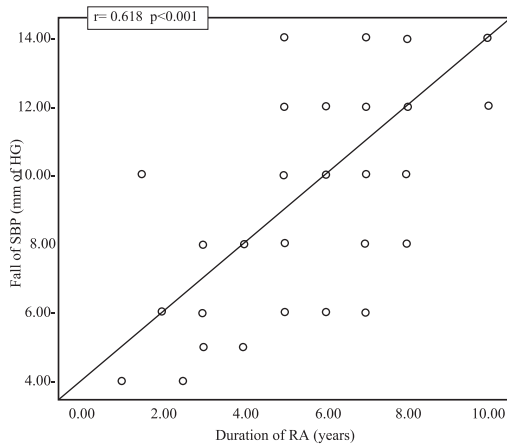
Variables	Control (n=30)	RA Patients (n=60)
Age (years)	36.50 $\pm$ 11.50 (18-65)	37.09 $\pm$ 11.10 (18-62)
BMI (Kg/m <sup>2</sup> )	23.88 $\pm$ 2.27 (20.07-28.57)	23.94 $\pm$ 1.68 (21.39-29.52)
Pulse (beat/min)	80.29 $\pm$ 10.62 (67-92)	85.34 $\pm$ 11.22* (68-99)
SBP (mm of Hg)	114.37 $\pm$ 11.79 (96-138)	116.19 $\pm$ 11.30 (96-138)
DBP (mm of Hg)	68.70 $\pm$ 7.59 (56-82)	73.77 $\pm$ 7.01*** (52-90)

Data were expressed as Mean  $\pm$  SD. Figures in parentheses indicate ranges. Statistical analysis was done by Independent sample t test. \* $p < 0.05$ , \*\*\* $p < 0.001$

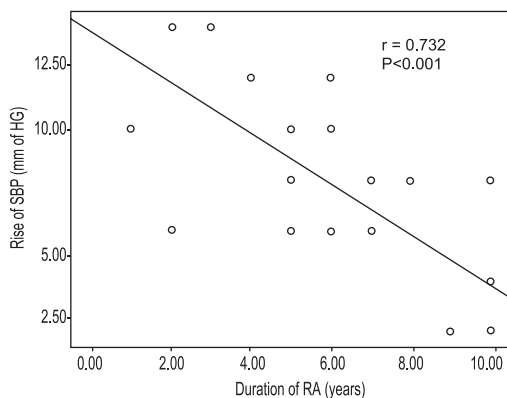
**Table II:** Sympathetic function parameters in two groups (n=90)

Variables	Control (n=30)	RA (n=90)
Fall of SBP (mm of Hg)	4.23 $\pm$ 2.06 (2-8)	8.68 $\pm$ 3.73*** (2-14)
Rise of DBP (mm of Hg)	18.37 $\pm$ 1.13 (12-20)	6.3 $\pm$ 2.84*** (2-12)

Data were expressed as Mean  $\pm$  SD. Figures in parentheses indicate ranges. Statistical analysis was done by Independent sample t test. SBP = Systolic blood pressure  
DBP = Diastolic blood pressure RA= Rheumatoid Arthritis, \*\*\* $p < 0.01$



**Figure 1:** Correlation of fall of SBP in response to standing with disease duration in RA patients is showing positive correlation with duration of RA which indicate more duration of disease greater fall of SBP in orthostatic test.



**Figure 2:** Correlation of rise of DBP in response to sustained handgrip with disease duration in RA is showing negative correlation which indicate rise of DBP lessened with duration of RA.

### Discussion

In this study, two non invasive cardiovascular reflex test, BP changes in response to postural challenge (fall. of systolic BP) and isometric exercise (rise of DBP) were used to assess the efficiency of sympathetic reactivity in RA.

The greater fall of SBP in orthostatic test and lesser rise of DBP in handgrip test in this study

demonstrated reduced sympathetic reactivity in RA patients. More over the significant negative correlation of this reduced response in hand grip and significant positive correlation of fall of SBP on standing to duration of rheumatoid arthritis suggest worsening of altered autonomic reactivity with duration of disease. It is also noteworthy that higher resting pulse rate, heart rate and diastolic blood pressure suggest lower parasympathetic or comparatively increased resting sympathetic tone in RA patients.

Several investigators assessed cardiovascular autonomic nerve function in RA patients and observed cardiovascular autonomic nervous system dysfunction<sup>5-8</sup>. Similar trends for greater fall of SBP in RA patients was noted by Louthreno et al<sup>5</sup>. and less rise of DBP was reported by Sandhu and Allen<sup>6</sup> whereas similar results in both parameters were also reported<sup>2</sup>.

In contrast Louthreno et al<sup>5</sup> found greater rise of DBP in response to sustained handgrip and also did not find any correlation between diminished blood pressure response and disease duration and between fall of SBP and orthostatic hypotension symptoms in RA patients. Sandhu & Allen<sup>6</sup> observed less fall of SBP in response to standing in patients with RA.

Leden et al<sup>8</sup> found increased resting heart rate in all 17 RA patients which was emphasized by Piha et al<sup>12</sup>. and Bidikar & Ichaporia<sup>2</sup>. Moreover, they found significant orthostatic hypotension with fall of SBP greater than 30 mm Hg in 8% and abnormal hand grip test in 30% RA patients.

The pathophysiology of the sympathetic dysfunction in RA is not yet clearly delineated. Immunological mechanism has been proposed for dysautonomia in RA<sup>5,13</sup>. Recently RA patients with autonomic dysfunction has been demonstrated with presence of autoantibody against nerve growth factor and cervical ganglion<sup>13-14</sup>. In the present study, the poor response of sympathetic nerve function to

orthostatic stress and isometric exercise reconfirm sympathetic dysfunction in RA which became worse with duration of disease. Thus RA patients are more vulnerable to cardiac morbidity & mortality due to sympathetic dysfunction especially in a situation of environmental challenge.

#### Conclusion:

In conclusion, sympathetic dysfunction occurred in RA patients which was deteriorated with duration of disease.

**Conflict of interest :** None

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