A comparative study of heart rate variability tests and lipid profile in healthy young adult males and females

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Abstract

Background: Coronary Heart Disease (CHD) is the leading cause of death in many developed countries. The relation between heart rate variability (HRV) and CHD was recently explored after the development of HRV techniques. Lower HRV was proven to be associated with a greater risk for developing hypertension among normotensive men, and hypertension is one of the major risk factors of CHD. Acute myocardial infarction is accompanied by decreased HRV, which is due to reduced vagal or increased sympathetic outflow to the heart.

Aim: This study was designed to test the hypothesis of influence of gender and lipid profile difference on heart rate variability tests.

Materials and Methods: Thirty healthy adult male and thirty healthy adult female subjects in the age group of 18-25 years without any addictions and gross systemic disease were selected. Heart rate variability tests during Valsalva maneuver, deep breathing and 30:15 R-R intervals ratio were carried and lipid profile of the subjects were analyzed.

Results: We found a decrease in values of HRV tests during the Valsalva maneuver, deep breathing in male individuals as compared with age- and Body Mass Index, BMI-matched females. VHeart Rate Variability tests during 30:15 R-R intervals Ratio in male individuals were significantly decreased as compared with females. Values of total cholesterol, Low Density Lipoprotein, LDL cholesterol were found to be significantly increased and High Density Lipoprotein, HDL cholesterol significantly decreased in males.

Conclusion: Healthy adult males may be at a higher risk of developing acute myocardial infarction and CHD due to decreased HRV and atherogenic lipid profile. Lower level of serum estrogen may be the cause of this difference in HRV among males. The difference in HRV tests among males and females disappears after menopause.

Key words: Coronary heart disease, diabetic auto neuropathy, gender influence and lipid profile, heart rate variability test

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Introduction

CHD is the leading cause of death in many developed countries. The relation between HRV and CHD was recently explored after the development of HRV techniques. Lower HRV was proven to be associated with a greater risk for developing hypertension among normotensive men, and hypertension is one of the major risk factors of CHD. Acute myocardial infarction (AMI) is accompanied by decreased HRV, which is due to reduced vagal or increased sympathetic outflow to the heart found in diabetic auto neuropathy (DAN). The relation of estrogen and CHD has been discussed in many studies. The cardiac vagotonic and sympatholytic effects of estrogen can explain that healthy adult males are at a higher risk of developing acute
myocardial infarction and CHD due to decreased HRV. Lack of estrogen in menopausal women may be a cause of difference in HRV among females. Lack of estrogen may cause autonomic dysfunction in males. The cardiac vagotonic and sympatholytic effects of estrogen can explain, at least in part, why premenopausal women compared with postmenopausal women have a lower CHD incidence and mortality rate. A metabolite of progesterone exerts a sympathoinhibitory effect and attenuates sympathetic baroreflex responses via a central mechanism.\(^1,2\) Hormonal factors may be a cause of variance in HRV tests among young adult males and females.\(^3\) Testosterone increases circulating levels of LDL cholesterol and decreases plasma HDL cholesterol. Estrogen is a sympathoinhibitor and vagotonic hormone. Estrogens have a significant plasma cholesterol-lowering action and they rapidly produce vasodilatation by increasing the local production of NO.\(^4\) Testosterone favors accumulation of upper body, abdominal and visceral fat.

The present study has been done to evaluate HRV tests and lipid profile in young males and females and to detect whether there is any significant difference between the two groups, so that early modification of lifestyle may prevent further morbidity and mortality.

### Materials and Methods

A total of 60 M.B.B.S students from Medical College, Kolkata were selected. Subjects were normotensive, non-obese and non-smokers. All subjects abstained from caffeine-containing beverages and alcohol during the study. None of the subjects had taken any regular medication, including oral contraceptives, for one year before the study period.

### Materials

Weighing machine, Height stand, 4-Channel Physiograph Polyrite- D. Manufactured by Records and Medicare Systems, RMS, Chandigarh, India, Measuring Tape and Sphygmomanometer. Auto analyzer (Hitachi-902) was used for Lipid Estimation.

### Anthropometry

Body weight and height were measured while Body Mass Index was calculated.

### Blood tests

Lipid profile was analyzed with automated analyzer from blood samples collected after 12 h of fasting.

### Heart rate variability tests

**Heart rate variations during Valsalva Maneuver**

The subject was instructed to exhale forcefully through the mouthpiece of the modified mercurial sphygmomanometer and to maintain pressure in the manometer up to 40 mmHg for 15 sec. Electrocardiogram, ECG recording was taken during the maneuver and continued for about 30 sec after the performance. The maneuver was repeated three times with a few minutes' time interval of rest. Nasal clip was used to stop nasal breathing of the subject during this maneuver. Calculation was done taking the ratio of the longest RR interval after blowing to the shortest RR interval during blowing. The highest ratio of the three maneuvers was used as the result of Valsalva ratio (VR).

**Deep Breath Test**

After a 5-min interval of rest in the supine position, the patient was instructed to take deep inspiration over 5 sec followed by expiration over the next 5 sec completing one respiratory cycle maintaining a tidal volume ranging between 1200 to 1500 ml. Six cycles were repeated in each test. The inspiratory and expiratory timings were synchronized by looking at the observer’s finger moving rhythmically up and down using a timer. The respiratory cycles were simultaneously recorded by the Polyrite-D. Calculation was done taking the mean of the maximum RR interval in the six expiratory cycles of the same tracing were calculated for heart rate during expiration. The difference of the heart rate between the maximum in the inspiratory cycles (I) and the minimum in the expiratory cycles (E) was calculated and was used as the result of HRV during deep breathing (HRDB), i.e., I – E difference or Deep Breath Difference (DBD).

30:15 R-R intervals Ratio were carried out with the help of Polyrite- D. After a complete rest of 15 min in the supine position, the ECG recording was started and the subject assumed erect posture from the supine position as quickly as possible (within 3 sec) with continuous ECG recording for 30 sec or more in erect posture. 30:15 ratio was calculated by taking the ratio of longest RR interval around 30th beat to shortest RR interval around 15th beat after standing.

### Statistical analysis

Results are expressed as mean ± SD. Difference between the groups was tested by Student's t-test. \(P\) value <0.05 was considered as statistically significant.

### Results

Mean value ± SD of Heart Rate Variability Tests’ Parameters and Lipid Profile Parameters are depicted in Table 1. The Valsalva Ratio was 1.384 ± 0.088 and 1.419 ± 0.1 in males and females respectively \((P = 0.079)\). Deep Breath Difference (beats/min) was 27.6 ± 5.2 and 29.06 ± 4.1 in males and females respectively \((P = 0.115)\). 30:15 R-R intervals ratio was 1.028 ± 0.01 in males 1.03 ± 0.12 and females respectively \((P = 0.035)\) and is of statistical significance. Serum cholesterol was found to be 162.5 ± 21.23 mg/dl in males and 153.667 ± 14.2 mg/dl in
females, \( P = 0.032 \) and is of statistical significance. Serum triglyceride levels were higher i.e., \( 112.63 \pm 25.7 \text{ mg/dl} \) in males than in females, \( 105.5 \pm 13.6 \text{ mg/dl} \), \( P = 0.093 \), but not statistically significant. HDL cholesterol was found to be lower \( (43.6 \pm 4.84 \text{ mg/dl}) \) in males compared with females \( (46.4 \pm 5.2 \text{ mg/dl}) \), \( P = 0.008 \) and is of statistical significance. LDL cholesterol was found to be higher in males, i.e., \( 75.06 \pm 12.8 \text{ mg/dl} \) compared with females \( (69.4 \pm 8.17 \text{ mg/dl}) \), \( P = 0.024 \) and is of statistical significance.

**Discussion**

The autonomic nervous system has two main divisions, the sympathetic and the parasympathetic. Many organs are controlled primarily by either the sympathetic or the parasympathetic division. Generally, the sympathetic division prepares the body for stressful or emergency situations i.e., the fight or flight. The parasympathetic division controls body processes during ordinary situations.

Baroreceptor reflex sensitivity has been found lower and heart rate variability has been found higher in healthy women than in men in studies by Serve et al., in 2001. They concluded that gender is an important determinant of baroreceptor sensitivity and heart rate variability. In 1996 S.M. Ettinger et al, concluded that sympathetic neuronal outflow is less in women compared with men. In 1994, Abdel Rahaman et al., first reported in healthy young subjects that females had lesser sensitivity of baroreceptor control of heart rate than males when blood pressure (BP) was acutely elevated by bolus intravenous injection of phenylephrine. B. Gautschy et al., in 1985 found significant difference in blood pressure responses to hand grip test and responses to hand grip were greater in men than in women. A more recent study in 2001 confirmed that cardiovagal reflex gain was less in female than male subjects, but the threshold, saturation operating range, and operating point were similar between male and female subjects. Gender difference in baroreflex-mediated bradycardic response is caused by the difference in the responsiveness of the parasympathetic component. Huihuru et al., in 1996 showed that baroreflex sensitivity determined by Valsalva maneuver was smaller in middle-aged women than age-matched men. In addition, their study demonstrated that vagally mediated baroreflex sensitivity was significantly greater in those with estrogen replacement therapy than in those without hormone replacement therapy in postmenopausal women, suggesting that plasma estrogen enhances vagal modulation of heart rate control. In rats, blockade of muscarinic receptors abolished the gender difference in baroreflex-mediated bradycardic

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Male subjects ( n=30 )</th>
<th>Female subjects ( n=30 )</th>
<th>( P ) value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Valsalva Ratio</td>
<td>1.384±0.088</td>
<td>1.419±0.1</td>
<td>0.079</td>
</tr>
<tr>
<td>Deep Breathing Difference (beats/min)</td>
<td>27.6±5.2</td>
<td>29.06±4.1</td>
<td>0.115</td>
</tr>
<tr>
<td>30:15 R-R intervals Ratio</td>
<td>1.028±0.01</td>
<td>1.03±0.12</td>
<td>0.035*</td>
</tr>
<tr>
<td>Cholesterol (mg/dl)</td>
<td>162.5±21.23</td>
<td>153.667±14.2</td>
<td>0.032*</td>
</tr>
<tr>
<td>Triglyceride (mg/dl)</td>
<td>112.63±25.7</td>
<td>105.5±13.6</td>
<td>0.093</td>
</tr>
<tr>
<td>HDL-Cholesterol (mg/dl)</td>
<td>43.6±4.84</td>
<td>46.4±5.2</td>
<td>0.008*</td>
</tr>
<tr>
<td>LDL-Cholesterol (mg/dl)</td>
<td>75.06±12.8</td>
<td>69.4±8.17</td>
<td>0.024*</td>
</tr>
</tbody>
</table>

*\( P \) value <0.05 (significant)
response, while B-adrenoreceptor blockade attenuated baroreflex-mediated bradycardia similarly in both genders, and the gender difference was still preserved.\(^\text{[11]}\) Christensen et al., in 1999 showed that hypercholesterolemia has been proved to be associated with a decreased 24-h HRV in men with or without coronary arterial disease.\(^\text{[12]}\) Chin- Hua Fu et al., in their studies in 2008 showed that baroreceptor sensitivity is negatively correlated with LDL cholesterol. The impaired endothelium-dependent arterial dilatation in vessel walls caused by higher lipid levels might also change the baroreflex capacity.\(^\text{[2]}\)

A previous study such as the ARIC study reveals that there is a relation of low HRV in both middle-aged men and women. This particular study also revealed that low HRV can predict the incidence of CHD. Previous studies with other methods of HRV tests such as Spectral analysis have also shown low HRV to predict incidence of CHD. Results of such a study confirmed the association over a longer follow-up period with the use of different methodologies and different subsets of ARIC Cohort.\(^\text{[13]}\)

This present study reveals that HRV decreases with age at a varying rate and to a different degree depending on the HRV Tests. It is further observed that HRV Tests revealed significant change in 30:15 R-R intervals Ratio in females compared with males as shown in graph 1 (\(P = 0.035\)). The mean values of Total Cholesterol, Triglyceride and LDL-Cholesterol were less in female subjects compared with males as shown in graph 2. Significant changes in LDL-Cholesterol and Total Cholesterol like this study were also seen in studies of Danev et al.,\(^\text{[14]}\) and Doncheva et al.,\(^\text{[15]}\) Hypercholesterolemia is associated with decreased 24-h heart rate variability and decreased heart rate variability is a strong predictor of CHD.\(^\text{[3]}\) Our findings are in agreement with the above mentioned previous studies. Mean values of HDL-Cholesterol were found to be higher in female subjects compared with male subjects. LDL is more directly associated with CHD. LDL is comprised of a spectrum of particles that vary in size, density, chemical composition and atherogenic potential. A preponderance of small, dense LDL is associated with an increased risk of myocardial infarction as well as the severity of CHD. The risk of CHD is 3-fold higher in women with small, dense LDL than in those with large buoyant LDL.\(^\text{[1]}\) The decrease of cardiac vagal activity and baroreflex sensitivity in females are related inversely to LDL cholesterol level. Increased LDL levels impair endothelium-dependent arterial dilation and change the baroreflex capacity.\(^\text{[2]}\)

Further research of HRV analysis and lipid profile taking into consideration the phases of the menstrual cycle is worth undertaking in future. This study has several limitations. Firstly, it is a cross-sectional study comprising a small group of 60 subjects with low mean age; therefore the directionality of associations between HRV and CHD cannot be clearly established. So large-scale clinical trials to establish a relation between elevated HRV and CHD are worth undertaking.

### Conclusion

The present study was done to evaluate HRV tests and lipid profile in young males and females and to detect the association if any with CHD. This study was also performed to evaluate whether there were any significant differences between the two groups, so that early modification of lifestyle may prevent further morbidity and mortality. The findings of this study indicate an association of altered sympathovagal activity with blood lipid concentrations. Autonomic dysfunction and atherogenic lipid profile in young adult males and females are major medical problems. Further understanding of the basic mechanism leading to autonomic dysfunction and atherogenic lipid profile in males and females may promote or guide more effective and rational choices of treatment.

Future research should focus on strategies to increase public awareness of the association of autonomic dysfunction and dyslipidemia with age among both males and females, including high-risk minority groups, to educate about and improve adherence to lifestyle modifications and to implement evidence-based medical practice.

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### References


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