ABSTRACT

Background:
Hypertension runs in families, and parental history of hypertension increases the risk of developing hypertension, especially if both the parents are hypertensive’s. In all, 25% of children with one hypertensive parent and 50% of children with two hypertensive parents will eventually become hypertensive demonstrating that heredity plays a major role in the development of the disease. The present study was undertaken to test the hypothesis that normotensive young male adults, with parental history of hypertension exhibit variations in cardiovascular autonomic functions as tested by the analysis of HRV with deep breathing.

Material and Methods:
The study group of 25 healthy normotensive male subjects whose parents are hypertensive, either father or mother or both being hypertensive but none being diabetic where as control group of 25 healthy normotensive male subjects whose parents were normotensive and non diabetic. All are aged between 18 to 25 years.

Results:
There was no significant difference in the anthropometric measurements and the resting parameters between the two groups (p>0.05). The Heart Rate Variability with Deep Breathing (HRVdb) was reduced in the study group when compared to the control group and was statistically significant (p<0.04).

Conclusions:
The study shows that HRV is reduced in normotensive young men with parenteral history of hypertension. Even though the baseline cardiovascular parameters values were normal in both the groups, it was by the way of recording of HRV with rest and the autonomic challenge by the way of the HRVdb the autonomic imbalance could be made out in the study group.

Key words: HRV db, Family history of Hypertension, Heart Rate, Blood pressure
INTRODUCTION:
Hypertension is the most common human cardiovascular disease. Worldwide it is estimated to cause 7.1 million premature deaths each year and 4.5% of the disease burden\(^1\).

Hypertension runs in families, and parental history of hypertension increases the risk of developing hypertension, especially if both the parents are hypertensive’s\(^2\). In all, 25% of children with one hypertensive parent and 50% of children with two hypertensive parents will eventually become hypertensive demonstrating that heredity plays a major role in the development of the disease\(^3\).

The ANS plays a fundamental role in the control of arterial blood pressure (BP) and, therefore, may be considered an important pathophysiologic factor in the development of arterial hypertension\(^4\). Normotensive subjects with family history of hypertension have greater sympathetic activity and also early parasympathetic attenuation\(^5\).

HRV has emerged as a practical, noninvasive tool to quantitatively assess cardiac autonomic dysfunction in hypertension\(^6\). Research into HRV and respiration over the past 150 years has led to the insight that HRV with deep breathing (HRVdb) is a highly sensitive measure of parasympathetic cardiac function. HRVdb is a reliable clinical test for early detection of cardio vagal dysfunction in a wide range of autonomic disorders\(^7\).

The present study was undertaken to test the hypothesis that normotensive young male adults, with parental history of hypertension exhibit variations in cardiovascular autonomic functions as tested by the analysis of HRV with deep breathing as compared to age and sex matched adults without family history of hypertension.

MATERIAL AND METHODS:
The present study was conducted in the Research laboratory in the Department of Physiology, Navodaya Medical College, Raichur, Karnataka.

The study group consisted of 25 healthy normotensive male subjects studying medical students (aged between 18 to 25 years) whose parents are hypertensive, either father or mother or both being hypertensive but none being diabetic.

The control group consisted of 25 healthy normotensive male subjects studying medical students (aged between 18 to 25 years) whose parents are normotensive and non diabetic.

The study was approved by Ethical Committee, Navodaya Medical College, Raichur.

**Inclusion Criteria** (common to both study and control groups)
- Healthy males in the age group of 18–25 yrs, non smokers, non alcoholic and normal range of BMI between 18.5 – 24.9 kg/m\(^2\)
- Parental hypertension > 10 yrs

**Exclusion Criteria** H/O any systemic disorders known to cause to autonomic dysfunction.

**Study Protocol**
The protocol was explained to the subjects and informed consent was obtained from each of the participant.
The participants were called between 10 to 12 AM after 2 hours of light breakfast. They were advised to avoid consumption of tea/coffee 12 hours prior to reporting in the laboratory. Upon arrival, the subjects were made to sit in the lab comfortably for 10 minutes to get accustomed to the new environment. Height in meters and weight in kgs were measured and BMI calculated. Then they were allowed to rest supine for fifteen minutes. The baseline RR, HR, SBP and DBP were recorded.

**Heart Rate Variability Analysis**

Recording were standardized and instructions followed as per the guidelines of Task Force of The European Society of Cardiology and The North American Society of Pacing and Electrophysiology.

A chest lead ECG was recorded using ECG V: 52 [HRV analysis software] for 5 minutes in supine rest with eyes closed, which is simultaneously analyzed by the software.

Beat-to-beat variations in instantaneous HR were derived offline using a rate-detector algorithm. For computing HRV indices during supine rest, recommendations of the Task Force on HRV were followed. Briefly, a 5-min ECG was acquired at a sampling rate of 1000 Hz during supine rest with the subjects breathing normally at 12–18 per min. RR intervals were plotted using the ECG V: 52 software. An RR series was extracted using a rate-detector algorithm after exclusion of artifacts and ectopic. A stationary 256 second RR series was chosen for analysis. In the time domain, the standard deviation of normal-to-normal RR intervals (SDNN) was taken as an index of overall HRV. Low frequency (LF) and high frequency (HF) spectral powers were determined by integrating the power spectrum between 0.04 and 0.15 Hz and 0.15 and 0.4 Hz respectively. Total power was calculated by integrating the spectrum between 0.004 and 0.4 Hz and includes very low frequency, LF and HF components. Spectral powers are expressed in absolute units of milliseconds squared. LF and HF powers are also expressed in normalized units.

**Heart Rate Response to Deep Breathing:**

The subject is trained to breathe deeply at a rate of 6 breaths/minute in supine position. The subject is asked to breathe deeply, steadily and slowly for 1 min at the rate of 6 breathes/min (5 sec inspiration and 5 sec expiration duration of each cycle of one minute) while ECG was continuously recorded. The HR change with deep breathing (deep breathing difference) was then expressed as the mean of the differences between the maximal and minimal HR in 6 respiratory cycles. Deep Breathing Difference (DBD) = Mean of HR Differences in 6 Breath Cycles.

**Statistical analysis:**

All data is expressed as Mean ± SD. Student ‘t’ test used to compare the data of both the groups. Mann-Whitney test used to analyze the Heart Rate Variability (HRV). The association between HRV and the variables (Age, BMI, Rest HR, SBP, and DBP) analyzed by stepwise multiple regressions. A p-value < 0.05 considered statistically significant and p value < 0.01 as statistically highly significant.

**Results:** There was no significant difference in the anthropometric measurements and the resting parameters between the two groups. The results are depicted in Table 1.
Table-1: Baseline Characteristics of Subjects (Mean ± SD)

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Study group</th>
<th>Control group</th>
<th>t-value</th>
<th>p-value</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>19.65 ± 1.63</td>
<td>18.90 ± 1.80</td>
<td>1.38</td>
<td>0.18</td>
<td>Not significant</td>
</tr>
<tr>
<td>BMI (Kg/m2)</td>
<td>21.85 ± 2.93</td>
<td>21.00 ± 1.64</td>
<td>1.13</td>
<td>0.27</td>
<td>Not significant</td>
</tr>
<tr>
<td>Resting RR breath/min</td>
<td>13.72 ± 0.6</td>
<td>14.02 ± 0.7</td>
<td>1.36</td>
<td>0.18</td>
<td>Not significant</td>
</tr>
<tr>
<td>Resting HR (bpm)</td>
<td>71.58 ± 5.48</td>
<td>75.66 ± 11.65</td>
<td>1.42</td>
<td>0.16</td>
<td>Not significant</td>
</tr>
<tr>
<td>Resting SBP (mm Hg)</td>
<td>121.70 ± 2.99</td>
<td>121.40 ± 6.8</td>
<td>0.18</td>
<td>0.86</td>
<td>Not significant</td>
</tr>
<tr>
<td>Resting DBP (mm Hg)</td>
<td>79.10 ± 2.63</td>
<td>77.30 ± 4.55</td>
<td>1.53</td>
<td>0.13</td>
<td>Not significant</td>
</tr>
</tbody>
</table>

Note: BMI - Body mass index, RR - Respiratory rate, HR - Heart rate, SBP - Systolic blood pressure, DBP - Diastolic blood pressure.

Heart Rate Variability (HRV) Parameters

The measured values of HRV parameters like Mean RRI, RMSSD, LF, LFnu, HF, HF nu and LF/HF among both the groups are presented in the Table-2. LFnu power indicating sympathetic activity were increased in the study group. HF & HFnu power indicating parasympathetic activity were decreased in study group. The LF/HF ratio indicating statistically sympathovagal balance was increased in study group. But the difference was not significant which exhibit little alteration in cardiovascular autonomic function.

Table-2: HRV Parameters (Mean ± SD) in Study group and Control group.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Study group</th>
<th>Control group</th>
<th>U-value</th>
<th>p value</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>MEAN RRI</td>
<td>767.45 ± 53.88</td>
<td>811.70 ± 115.61</td>
<td>147.5</td>
<td>0.13</td>
<td>Not significant</td>
</tr>
<tr>
<td>RMSSD</td>
<td>23.66 ± 5.02</td>
<td>27.25 ± 9.96</td>
<td>173.5</td>
<td>0.16</td>
<td>Not significant</td>
</tr>
<tr>
<td>LF</td>
<td>908.95 ± 122.07</td>
<td>986.85 ± 168.62</td>
<td>133.5</td>
<td>0.10</td>
<td>Not significant</td>
</tr>
<tr>
<td>LF nu</td>
<td>68.10 ± 3.7</td>
<td>65.26 ± 7.07</td>
<td>152.5</td>
<td>0.12</td>
<td>Not significant</td>
</tr>
<tr>
<td>HF</td>
<td>445.48 ± 46.35</td>
<td>474.68 ± 58.48</td>
<td>147.0</td>
<td>0.09</td>
<td>Not significant</td>
</tr>
<tr>
<td>HF nu</td>
<td>31.9 ± 1.90</td>
<td>33.08 ± 1.97</td>
<td>128.55</td>
<td>0.07</td>
<td>Not significant</td>
</tr>
<tr>
<td>LF/HF</td>
<td>2.06 ± 0.38</td>
<td>2.10 ± 0.42</td>
<td>183.5</td>
<td>0.08</td>
<td>Not significant</td>
</tr>
</tbody>
</table>
RMSSD: Root mean square successive difference in milliseconds, LF: Low frequency, LF nu: Low frequency in normalized units, HF High Frequency, HFnu: High Frequency in normalized units, LF/HF: Low frequency/High Frequency ratio.

**HRV with Deep Breathing:**
The measured value of Inspiration-Expiration (I-E) HR difference with deep breathing in Study group and Control group subjects, expressed as Mean ± SD is presented in the Table-3.

**Table-3:** HRVdb (Mean ± SD) in Study group and Control group

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Study group</th>
<th>Control group</th>
<th>U-value</th>
<th>p value</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>HRVdb</td>
<td>25.05 ± 2.46</td>
<td>27.70 ± 3.98</td>
<td>113.0</td>
<td>0.04</td>
<td>Significant</td>
</tr>
</tbody>
</table>

The Heart Rate Variability with Deep Breathing (HRVdb) was reduced in the study group when compared to the control group and was statistically significant (p<0.04).

**Discussion:**
Both groups in this study consisted of age, sex, and BMI-matched, young, normotensive male subjects. They differed only in the genetic propensity for developing hypertension later in life. Although the resting heart rate, systolic and diastolic blood pressures were found to be higher in subjects of study group as compared with control group this difference was statistically insignificant (p>0.05) (Table I). This shows that both the groups are normotensive at rest.

Similar baseline characteristics were observed in studies done by Chinagudi. S et al⁹ and Rathi. P et al¹⁰. This may be due to the younger age group and the BMI was within normal limits.
However studies done by Lopes et al\textsuperscript{11} and Ostfeld et al\textsuperscript{12} report a slightly elevated pressure blood in normotensive subjects with a family history of parental hypertension. This blood pressure elevation may be considered as a permanent abnormality characterizing a prehypertensive stage early in life\textsuperscript{13}. Study done by Julis et al opines that those with parental history of hypertension their offspring show higher resting diastolic pressure probably due to hyperactive sympathetic nervous system (SNS)\textsuperscript{14}.

**Measures of Heart Rate Variability (HRV):**
The time domain methods are used to investigate recordings of short durations, whereas the frequency domain methods are usually able to provide results that are more easily interpretable in terms of physiological regulations.

In our study the measures namely the time domain measures of HRV, the Mean RRI and RMSSD were reduced in the study group when compared to the control group. The Mean RRI measures the sum of the levels of parasympathetic and sympathetic influences and RMSSD reflects an estimate of parasympathetic regulation of the heart\textsuperscript{15}.

Also among the frequency domain measures of HRV our study showed us that there is LFnu and decreased HFnu and increased LF/HF ratio in the study group when compared with controls. Similar results have been reported by other investigators\textsuperscript{9,16,17}. LFnu reflects the sympathetic activity while HFnu is the direct representation of vagal tone and LF/HF ratio is an indicator of sympathovagal imbalance\textsuperscript{15}. These findings indicate that there is increased sympathetic activity and decreased parasympathetic activity in the study group when compared with the control group.

**Heart Rate Variability with Deep Breathing (HRVdb):**
In our study the Heart Rate Variability with Deep Breathing (HRVdb) was reduced in the study group when compared to the control group and was statistically significant. Similar result was observed in the study done by Krishnan et al\textsuperscript{17}

Deep breathing induced changes in HR occur because of alterations in cardiac parasympathetic activity and when this system is impaired deep breathing leads to decrease in HRV.

Three mechanisms are generally proposed to explain the modulation of HR associated with respiration:

1. A direct influence of medullary respiratory neurons on cardio motor neurons;
2. An indirect influence on heart rate of blood pressure changes secondary to respiratory movements that are mediated via arterial baroreceptors or atrial stretch receptors;
3. A reflex response to lung inflation mediated by thoracic stretch receptors, most likely from the lungs and chest wall.

In most autonomic disorders, parasympathetic function is affected before sympathetic function, so HRVdb provides a sensitive screening measure for parasympathetic dysfunction in many autonomic disorders\textsuperscript{18}.

**Conclusion:**
In conclusion, this study shows that HRV is reduced in normotensive young men with parenteral history of hypertension. Even though the baseline cardiovascular parameters values
were normal in both the groups, it was by the way of recording of HRV with rest and the autonomic challenge by the way of the HRVdb the autonomic imbalance could be made out in the study group. Since the subjects are young, the autonomic imbalance in them suggests that tendency for developing hypertension sets in at an early age. So in such individuals the regular monitoring of autonomic activity by simple noninvasive recording of HRV and by simple parasympathetic test like HRVdb may prove to be a useful tool in predicting the future hypertensive. Also as a preventive measure, the predisposed group should aim at decreasing the sympathetic drive and increasing their parasympathetic drive which can be achieved by lifestyle modifications and slow breathing exercises\textsuperscript{12,13}.

REFERENCES:


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13. Steve Julius, Autonomic Nervous System Dysregulation in Human Hypertension; Am J Cardiol 1661; 67:36-7B).


