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# The Role of Autonomic Dysregulation in Newly Diagnosed Hypertension

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**Abstract:** Number of studies have established the role of the autonomic dysregulation in established hypertension, but only few have evaluated autonomic dysregulation in newly diagnosed hypertensive individuals. We hypothesized that autonomic dysregulation not only plays a role in the progression of hypertension but also in the onset of the same. We tested the hypothesis in 30 newly diagnosed hypertensive individuals by recording Heart Rate Variability at supine rest for 20 minutes using RMS Polyrite D hardware 2.2 (India) and compared with age and gender matched normotensive controls. During supine rest compared to the controls, mean RR was significantly reduced in the hypertensives ($p < 0.01$**), LF/HF ratio was significantly increased in the hypertensives ($p< 0.05$*). LF in n.u. was non significantly increased in the hypertensives. HF in n.u was significantly reduced in the hypertensives ($p< 0.05$*).Time domain measures for the hypertensives showed highly significant reduction in SDNN, RMSSD, pNN50 and NN50 count ($p < 0.01$**) when compared to controls. All these observations are a pointer towards a reduced parasympathetic activity in the hypertensives and an increase in sympathetic activity which might be due to the centrally originating oscillations to the heart and blood vessels. In conclusion, Autonomic dysregulation occurs not only in clinically established hypertensives but also in newly diagnosed hypertensives at the time of diagnosis as well.

**Key words:** Autonomic Dysregulation, Hypertension, Heart Rate Variability

## INTRODUCTION

**Hypertension Is an Increasingly Important Medical and Public Health Issue:** Data from observational studies involving more than 1 million individuals have indicated that death from both ischaemic heart disease (IHD) and stroke increases progressively and linearly from levels as low as 115 mmHg systolic blood pressure (SBP) and 75 mmHg diastolic blood pressure (DBP) [1]. Autonomic nervous system plays an important role in blood pressure regulation and in the development of hypertension. (Julius S. *et al* 1991) [2]Cardiovascular autonomic regulation plays an important role in cardiac mortality in various patient populations [3-7]. The autonomic nervous system influences blood pressure and heart rate through adjustments in parasympathetic and sympathetic activity. Parasympathetic and sympathetic activities are tightly regulated through baroreflex mechanisms [8]. Baroroeflexes have a pivotal role in short term cardiovascular regulation and buffer excessive blood pressure swings. [9, 10]. Among numerous other variables, baroreceptor reflexes are also involved in long term blood pressure maintenance. [11-13]. Heart Rate Variability (HRV) is a simple non-invasive tool to evaluate the cardiac autonomic function. Reduction in HRV is associated with an increase in cardiac mortality and has been shown to predict risk of cardiac events [14, 15].

Although a number of studies have established the role of the autonomic dysregulation in established hypertension there is paucity of studies that have evaluated the autonomic dysregulation in newly diagnosed hypertensive individuals.

We hypothesized that autonomic dysregulation not only plays a role in the progression of hypertension but also in the onset of the same. We tested the hypothesis in newly diagnosed hypertensive individuals using HRV at supine rest for 20 minutes.

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## MATERIALS AND METHODS

**Subjects:** 30 Newly diagnosed hypertensive individuals based on JNC criteria 7th Annual report [16] ( both genders included), were selected on random basis from the Hypertension clinic of Stanley Medical College and Hospital and compared with age and gender matched healthy normotensive controls.

**Protocol:** Instititutional ethical committee approval was obtained before the study. Written and informed consent was obtained from all the individuals who participated in the study.

The tests were performed in the Neurophysiology lab of the Department of Physiology, Stanley Medical College, Chennai-1 between 10 AM and 1 PM. The lab environment was quiet, the temperature was maintained between 25 to 28°C and the lighting subdued. Subjects were asked to empty their bladder before the tests. The test did not involve any intravascular instrumentation or administration of any drugs at any stage.

**HRV Analysis:** The recommendations of the task force 1996 [17] were followed for HRV recording. ECG was acquired using RMS Polyrite D hardware 2.2 (India). An RR series was extracted from ECG using maximum amplitude and sharpness of the peaks for R wave detection, these are RMS proprietary algorithms and validated with Fluke Biomedical, USA. After exclusion of artifacts and ectopics a stationary 256s RR series was chosen and analysed using RMS 2.5.2 software on a Microsoft window based PC. Respiratory movements were recorded using respiratory belt which analyses inspiration and expiration. BP was recorded using mercury spghmomanometer. Time domain analysis was used for long term HRV changes and frequency analysis was used for short term HRV changes.

**Statistical Analysis:** The variation between the two groups was tested using student independent unpaired 't' test. Statistical package for social analysis SPSS software 11.5 version was used for statistical analysis. $p< 0.05$* was taken as significant.

## RESULTS

There was no statistical difference between the control and the study group with regards to the age and BMI (P>0.05). (Table 1). Compared to the controls, Resting heart rate was increased significantly in the hypertensives ($p < 0.01$**) SBP, DBP, PP were significantly elevated in the hypertensives ($p<0.01$**) as notified in Table 2.

During supine rest, mean RR was significantly reduced in the hypertensives ($p < 0.01$**). In the frequency domain measures during supine rest hypertensives LF in absolute power was non significantly

Table 1: Anthropometry of subjects (Age, BMI expressed as mean ± SD)

| | Group ( n =30) {M=25 F=5} | Mean | Standard Deviation(SD) | Student independent t test |
|---|---|---|---|---|
| Age in years | Case | 44.06 | 5.48 | p = 1.00 |
| | Controls | 44.06 | 5.45 | |
| Body mass Index in Kg/m2 | Case | 23.81 | 3.72 | p = 0.840 |
| | Controls | 24.02 | 4.52 | |

Table 2: Comparison of Resting Heart Rate and blood pressure expressed as mean ± SD

| | Group ( n =30) {M=25 F=5} | Mean | Standard Deviation(SD) | Student independent t test |
|---|---|---|---|---|
| Resting Heart Rate In bpm | Case | 78.00 | 11.31 | p < 0.01** |
| | Controls | 68.4 | 8.6 | |
| SBP mmHg | Case | 158.00 | 17.72 | p < 0.01** |
| | Controls | 113.00 | 18.03 | |
| DBP mmHg | Case | 99.53 | 10.01 | p < 0.01** |
| | Controls | 75.86 | 9.49 | |
| PP mmHg | Case | 58.46 | 16.52 | p < 0.01** |
| | Controls | 37.13 | 11.11 | |
| MAP mmHg | Case | 119.02 | 10.53 | p < 0.01** |
| | Controls | 88.24 | 11.87 | |

SBP-Systolic Blood Pressure, DBP, Diastolic Blood Pressure, PP-Pulse Pressure, MAP-Mean Arterial Pressure, bpm-beats per minute.

Table 3: Changes in Frequency Domain measures between the two groups during supine rest

| | Case n=30 | | Control n=30 | | |
|---|---|---|---|---|---|
| Frequency Domain Measures | Mean | SD | Mean | SD | Student independent t test |
| Mean RR in sec | 0.78 | 0.12 | 0.88 | 0.10 | p < 0.01** |
| LF in ms² | 12.67 | 10.37 | 10.23 | 6.64 | p=0.282 |
| HF in ms² | 5.67 | 5.63 | 9.35 | 11.21 | p= 0.109 |
| LF/HF | 3.24 | 2.65 | 1.91 | 1.04 | p< 0.05* |
| TOTAL POWER ms² | 18.29 | 15.45 | 19.58 | 15.55 | p = 0.748 |
| LF in n.u. | 68.11 | 16.60 | 60.46 | 17.12 | p = 0.084 |
| HF in n.u | 29.46 | 12.19 | 39.63 | 17.07 | p< 0.05* |

LF-Low frequency HF-high frequency

Table 4: Changes in Time Domain measures between the two groups during SUPINE REST

| | Casen=30 | | Control n=30 | | |
|---|---|---|---|---|---|
| Time Domain Measures | Mean | SD | Mean | SD | Student independent t test |
| SDNN in ms | 26.58 | 15.80 | 57.78 | 21.30 | p < 0.01** |
| RMSSD in ms | 20.96 | 14.26 | 55.85 | 35.27 | p < 0.01** |
| NN50 count | 22.03 | 40.84 | 88.53 | 62.17 | p < 0.01** |
| pNN50 % | 6.36 | 11.72 | 28.03 | 21.49 | p < 0.01** |

SDNN -Standard Deviation of average Normal to Normal RR intervals; RMSSD Root Mean of the Sum of Squares of Difference between adjacent NN intervals; NN50 Normal to Normal RR interval deviation more than 50ms; pNN50 -the proportion of NN50 divided by total number of NNs.

increased and also HF in absolute power was non significantly reduced in the hypertensives. LF/HF ratio was significantly increased in the hypertensives (p< 0.05*). LF in n.u. was non significantly increased in the hypertensives. HF in n.u was significantly reduced in the hypertensives (p< 0.05*) compared to controls. (Table 3).

Time domain measures during supine rest for the hypertensives showed reduction in SDNN, RMSSD, pNN50 and NN50 count which was highly significant (p<0.01**) when compared to controls (Table 4).

## DISCUSSION

The present study demonstrated a significant increase in the Resting heart rate (RHR) in the hypertensive subjects. This is similar to the findings observed in Singh *et al* 1998 [18] which might be due to an increase in centrally originating oscillations in sympathetic drive to the heart. Previous studies have also suggested a parasympathetic inhibition and /or a sympathetic stimulation to the heart in hypertensive subjects [19-21].

Since variance is mathematically equal to total power of spectral analysis. The variations in heart rate may be evaluated by a number of methods. Perhaps the simplest to perform are the time domain measures. The simplest variable to calculate is the standard deviation of the NN intervals (SDNN), that is, the square root of variance. There is clear evidence of a significant difference in overall heart rate variability as measured by SDNN. Also, HF power at rest is decreased in respiratory sinus rhythm in newly diagnosed hypertensives. HF n.u. is significantly decreased in hypertensives (p <0.05*). There is significantly greater low frequency modulation of heart rate at rest in newly diagnosed hypertensives, this measured in terms of absolute units of power. SDNN reflects all the cyclic components responsible for variability in the period of recording. The SDNN was significantly decreased in the hypertensives (p < 0.01**). The findings are in accordance with Radaelli *et al* 1994 [22], Huikuri *et al* 1996 [23] Singh *et al* 1998 [18]; E.S. Prakash *et al* 2005 [24]. pNN 50 and RMSSD are measures of high frequency variations in HR and are highly correlated ( TASK FORCE REPORT 1996). In our observations the RMSSD and pNN50 were significantly reduced (p<0.01**) in the hypertensives. This is in accordance with Singh *et al* 1998 [18]. NN50 count was also reduced significantly in the hypertensives (p< 0.01**). All these observations are a pointer towards a reduced parasympathetic activity in the hypertensives.

Mechanisms influencing heart period modulation can be assumed to be stationary in short term recordings (Task force report, 1996) [17]. HRV occurring in the frequency range 40-400 mHz is mainly due to two mechanisms-tonic vagal activity and reflex vagal activity. It is important to appreciate that power in this range signifies the extent to which HR is modulated by

acetylcholine released upon stimulation of cardiac vagal nerves. It is an index of parasympathetic modulation of instantaneous heart rates and is also dependent upon the sensitivity of effectors to acetylcholine. It does not quantify and may not correlate with vagal nerve traffic.

Although not significant the LF in absolute power was increased in the hypertensives The LF/HF ratio was significantly increased in the hypertensives. ($p<0.05$*). LF n.u. is non significantly increased in hypertensives, this finding is in contrary to that reported in ES Prakash *et al*. [24]. Also, the LF nu in newly diagnosed hypertensives at rest is significantly greater compared to non hypertensive. Baroreflex mediated LF fluctuations in HR buffer oscillations in arterial pressure occurring at about the same frequency [25]. Therefore, an increase in the absolute power of LF oscillations in HR suggest that blood pressure fluctuations are occurring at that same frequency-these may in turn be due to centrally originating oscillations in sympathetic effects on blood vessels. This may effectively indicate greater BP liability in newly diagnosed hypertensives.

**Study Limitations:** From the study it is proved beyond doubt that autonomic dysregulation plays a key role not only in the maintenance of hypertension but also in its onset. However the study tested autonomic function in newly diagnosed hypertensive individuals using HRV analysis in supine rest for 20 minutes alone. Since Baroreceptors play a key role in the short term blood pressure regulation, the study could be expanded by using passive tilt/ active standing in these individuals to assess the baroreflex sensitivity in these individuals to confirm the role of autonomic dysregulation in the study group.

## CONCLUSION

Autonomic dysregulation occurs not only in clinically established hypertensives but also in newly diagnosed hypertensives at the time of diagnosis as well. Heart rate variability is a simple non-invasive test which could be used to detect the autonomic dysregulation in the hypertensives. In the future HRV can be used along with blood pressure measurements in the screening as well as management of hypertension.

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