



STUDY OF HEART RATE VARIABILITY AMONG HYPERTENSIVE PATIENTS OF RURAL SOUTH KERALA

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ABSTRACT

Introduction: Cardiac autonomic dysfunction due to hypertension (HTN) is high in developing countries like India and heart rate variability (HRV) tests help in the early detection and prevention of mortality and morbidity. The objective was to study the HRV among patients with hypertension attending a primary health centre in comparison with normal control group. **Methods:** The cross sectional study included 98 adult subjects in the age group of 30–60 years attending a primary health centre in South Kerala. Participants were divided into 2 groups and sampling was done based on the inclusion and exclusion criteria. 5 min ECG recording connected to a 16 channel polygraph machine was done for HRV analysis. The procedure was done with informed and written consent. Data was analyzed using HRV analysis software and statistical significance was set at $p < 0.05$. **Results:** Statistically significant difference in HRV parameters were observed among the participants. **Conclusion:** There is significant impairment in cardiac autonomic function among hypertensive patients when compared to normal subjects, which is characterized by decreased HRV and lower parasympathetic activity. This accentuates the importance of early assessment of autonomic function tests so as to reduce cardiovascular morbidity and mortality.

KEYWORDS : cardiac autonomic function, heart rate variability (HRV), hypertension (HTN)

INTRODUCTION

Hypertension is the most common disease, which doubles the risk of cardiovascular morbidity and mortality. It accounts for 20-50% of all deaths. Hypertension damages blood vessels, retina, heart, kidneys and nervous system.

Genetic factors play a crucial role, comprised of approximately 40-60% of cases. Environmental factors include high salt intake, heavy consumption of alcohol, obesity and lack of exercise etc. A systematic review and meta-analysis by Nupane et al. discussed the hypertension prevalence rate for several Asian countries - Bangladesh: 17.9%; Bhutan: 23.9%; India: 31.4%; Maldives: 31.5%; Nepal: 33.8%; Pakistan: 25%; and Sri Lanka: 20.9%.

A recent study from Kerala, India showed a higher prevalence of hypertension.⁽¹⁾

Heart rate Variability (HRV) is the physiological phenomenon of variation in the time interval between heartbeats. The SA node which generates the normal heart rate, receives several different inputs and the instantaneous heart rate or RR interval and its variation are the results of these inputs. Heart rate variability tests are non-invasive tests for studying the cardiac autonomic dysfunction in patients with hypertension and its implementation would help for early detection and help to reduce the mortality in patients.

This particular study is to hypothesize whether hypertension has an additive or synergistic role in affecting the cardiovascular system and in hastening autonomic dysfunction.

MATERIALS AND METHODS

Study Design: Cross sectional study

Study Duration: 12 months after obtaining Ethics Committee approval

Study Setting: Primary health centre, Alappuzha

Sample Size

The sample size is calculated according to the formula:- $n = (Z\alpha + Z1 - \beta) \times SD2 \times 2$

d2

d = effect size

$Z\alpha = 1.96$

$SD = 14.1$ (The standard deviation was taken from H.Kudatli et al. in his study on Heart rate variability in Diabetes Patients)

$Z1 - \beta = 0.84$

$n = 49$ in each group

i.e total sample size was 98

Study Population

Patients with hypertension between the age group of 30-60 years attending Primary health centre, South Kerala and healthy controls.

Inclusion Criteria

In control group normal healthy individuals without any comorbidities were selected.

Known hypertensives on treatment and within duration of 10 years from diagnosis was selected.

Exclusion Criteria

Subjects with history of coronary heart disease, congestive cardiac failure, arrhythmias, thyroid disorders, tumours, history of tobacco and alcohol consumption or any other systemic or debilitating disease, non consenting people were excluded

Study Variables

1. Age
2. Gender
3. Systolic pressure (mmHg)
4. Diastolic pressure (mmHg)
5. Heart rate variability – time and frequency domain analysis

Time Domain

1. MNN – mean R-R interval(ms)
2. SDNN – standard deviation for normal R-R interval(ms)
3. RMSSD – square root of mean of squares of differences between successive R-R interval(ms)
4. Pnn50 – percentage of consecutive RR intervals that differ by >50 ms(%)
5. NN50 count – number of RR intervals that differ by >50ms

Frequency Domain

1. LF(nu) – Low frequency normalized units
2. HF(nu) – High frequency normalized units
3. LF/HF ratio

Data Collection Tools

1. Proforma
2. 16 channel polygraph machine (PHYSIO-PAC 16)
3. HRV analysis software version 1.1
4. Mercury sphygmomanometer

PHYSIO-PAC 16 : It is a 16 Channel computer based Polygraph Machine, capable of simultaneously recording signals in the different modes from many sources.

HRV Analysis Software version 1.1, a product of Biomedical Signal Analysis Group, Department of Applied Physics, University of Kuopio, Finland was used for analysis of the ECG recording for Heart rate Variability.

Data Collection Procedure

After obtaining Institutional Research Committee and Ethics Committee approval, the study was conducted at Primary health centre, Alappuzha.

After obtaining the written consent, the participants were advised to rest for 10 minutes in supine position before evaluating their blood pressure and performing heart variability tests. Bloodpressure was then recorded in right arm in supine position using a mercury sphygmomanometer.

Four ECG limb leads connected to the polygraph machine were placed on each limb of the subjects in supine position and then the subjects were advised to close their eyes and breathe normally following which the ECG was recorded for 5 minutes.

After the ECG recording, HRV analysis of ECG was exported and analyzed using HRV analysis software version 1.1

Following HRV parameters were analysed in this study :**Time domain**

1. SDNN- standard deviation of normal R-R interval (ms)- that reflects the overall HRV
2. RMSSD- square root of mean squared differences between successive RR interval (ms)- that reflects the cardiac vagal modulation.
3. NN50 count- number of pairs of adjacent NN intervals differing by more than 50ms in entire recording – that reflects parasympathetic activity
4. NN50 (the proportion of differences in consecutive NN intervals that are longer than 50 ms) – its significance is similar to RMSSD

Frequency Domain

1. LF power- low frequency (0.04-0.15Hz); in nu- reflects predominantly the sympathetic modulation
2. HF power- high frequency (0.15- 0.4Hz); in nu- indicates the cardiac vagal modulation
3. LF/HF- ratio of absolute LF power to HF power- suggestive of sympathovagal balance

Normalized units (nu) and LF/HF ratio allow for an accurate assessment of the balanced modulation of each branch of ANS while not being influenced by the total power within the power spectrum.

Statistical Analysis

The data was entered in Microsoft Excel 2010 and analyzed by SPSS (version 17) for windows. Results were summarized in tables and figures. Data was expressed as mean $\pm$ standard deviation. Statistical difference in variables among groups were tested either using one-way ANOVA or unpaired t-test.

Pearson's correlation coefficients were estimated to correlate HRV parameters with age. Statistical significance was considered to be $p < 0.05$

Ethical Considerations

Confidentiality was maintained during all stages of the study.

No expenses were incurred on the part of the study participants for the purpose of the study.

Budget

There was no financial burden for the subjects

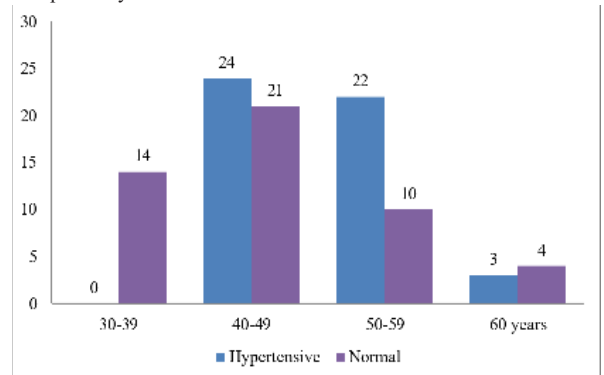
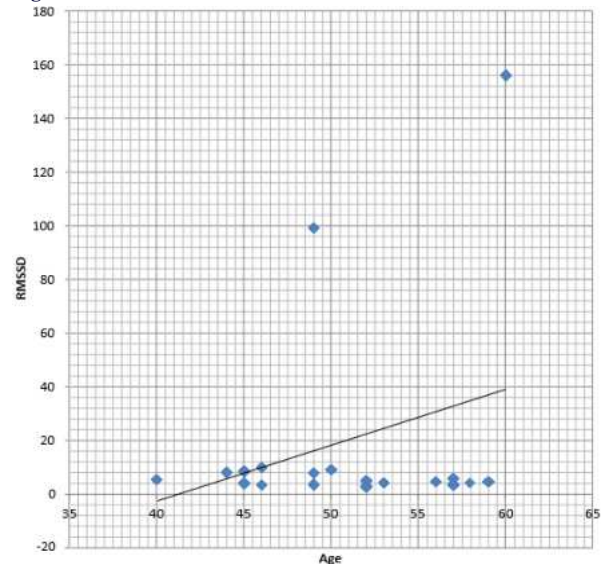
RESULTS

There was a female predominance among the study population and a variation among the average age of hypertensive subjects and normal controls as seen in Table 1

The majority of the hypertensive subjects and normal controls were between the age of 40-49 years as shown in Figure 1

There was a significant positive correlation between RMSSD and age in subjects with hypertension as shown in Figure 2

Among time domain HRV indices, SDNN (ms) and RMSSD (ms) were found to be significantly lower while frequency domain HRV indices were found to be statistically insignificant in hypertensive subjects when compared to normal control group as shown in Table 2 and Table 3 respectively.

**Figure 1****Figure 2:** Scatter plot diagram showing statistically significant positive correlation between RMSSD and age in subjects with hypertension $r = 0.283$; p value 0.049**Table 1: Comparison Of Demographic Variables Among Individuals With Hypertension And Normal Group**

Sl. No	Variables	Hypertension	Normal
1	Gender (m/f)	5/44	16/33
2	Age (years)	51.08 $\pm$ 5.70	44.71 $\pm$ 8.84
3	Duration (years)	4.653 $\pm$ 3.139	-
4	Systolic Blood Pressure (mmHg)	128.82 $\pm$ 17.35	111.22 $\pm$ 9.92
5	Diastolic Blood Pressure (mmHg)	79.02 $\pm$ 7.91	75.88 $\pm$ 7.85

The demographic variables were found to be statistically significant ($p < 0.0001$) by one way ANOVA test.

Table 2 : Comparison Of Time Domain HRV Indices Between Normal Group And Hypertension Group By Unpaired T Test

Sl. No.	Time domain indices	Normal	Hypertension	p value
1	MNN(ms)	0.473 $\pm$ 0.288	0.467 $\pm$ 0.155	0.897

2	SDNN(ms)	0.091±0.159	0.032±0.060	0.017
3	RMSSD(ms)	51.304±87.080	20.380±41.785	0.028
4	PNN50(%)	4.114±6.972	4.379±11.375	0.891
5	NN50 count	3.224±5.137	3.426±8.742	0.891

Table 3: Comparison Of Frequency Domain HRV Indices Between Normal Group And Hypertension Group By Unpaired T Test

Sl. No.	Frequency Domain Indices	Normal	Hypertension	p value
1	LF	56.782±16.492	59.658±16.912	0.396
2	HF	43.218±16.492	40.342±16.912	0.396
3	LF/HF ratio	1.688±1.114	2.089±1.679	0.166

DISCUSSION

Hypertension is the most common human cardiovascular disease and is characterized by systolic blood pressure (SBP) of more than 140 mmHg and/ or diastolic blood pressure (DBP) of >90 mmHg (2). In more than 95% of cases, a specific underlying cause of hypertension cannot be found and such patients are said to have essential hypertension. The pathogenesis of essential hypertension is not clearly understood but is believed to be attributed to renal, neurogenic, vascular and genetic factors.(3)

Heart rate variability (HRV) is a simple non-invasive technique used to assess the instantaneous beat-to-beat variations in terms of R-R interval length. (4). It is a measure of balance within the autonomic nervous system (ANS) of the sympathetic (SNS) and parasympathetic (PSNS) nervous systems. Reduced HRV is a marker of ANS dysfunction, and occurs in conditions like diabetes and hypertension (5).

Assessment of heart rate variability (HRV) is based on the analysis of consecutive sinus rhythm R-R intervals and may provide quantitative information about the modulation of cardiac vagal and sympathetic nerve activities. HRV measurements can be derived from short term (2 to 5 minutes) or long-term ECG recordings (24 to 48 hours). It can be quantified in a number of ways but the predominantly utilized conventional techniques are the time domain (statistical and geometrical) and frequency domain measurements (power spectral density) (6).

As clearly demarcated in the results section, it is evident that there was a female predominance (90%) compared to males (10%) which is similar to the previous studies conducted by J.D. Solanki et al. , Singh et al and Zhang et al (7,8)

Among the HRV parameters in time domain indices, SDNN (ms) (standard deviation of normal to normal intervals) and RMSSD (ms) (square root of mean squared differences of successive NN intervals), were decreased in the hypertension group when compared to normal group which is in agreement with the literature. Schroeder et al suggested that heart rate variability will be reduced uniformly in mild to moderate untreated hypertension (9).

SDNN and RMSSD are suggestive of the overall heart rate variability and parasympathetic activity to heart respectively. Reduction in SDNN and RMSSD in hypertensive subjects can be due to the impaired regulation of ANS which plays a role in the pathogenesis of hypertension. The frequency domain indices were found to be insignificant which is in contradiction to few other studies.

The time domain indices investigate the recordings of short durations and frequency domain indices provide results in terms of physiological regulations.

Time domain indices record the heart rate at any point in time or the intervals between successive QRS complex in a continuous ECG record. Present study showed decreased value of RMSSD which indicates decreased heart rate variability, suggestive of decreased vagal modulation and higher sympathetic activity in hypertension. RMSSD which is an estimate heart rate in short term NN recordings, reflects the parasympathetic regulation of the heart. Reduced HRV is associated with cardiac arrhythmias and it shows a risk factor for hypertensives. The frequency domain indices found to be insignificant in hypertensive group when compared to normal group in the present study could be explained by variations in response of neural regulatory mechanisms.

Previous studies in large population using heart rate variability have demonstrated reduced HRV indices in contrast to the present study.

Even though present study did not show significance in HRV indices compared to that normal.

Pearson Correlational analyses with age and time domain indices showed statistically significant positive correlation with RMSSD in subjects with hypertension.

Although our results did not allow us to conclude much on sympathetic activity, presence of parasympathetic impairment was noticed in subjects with hypertension as the overall heart rate variability was low. So it is possible that autonomic dysfunction may play a role in the pathogenesis of these disease conditions as sympathetic activity gets dominated to compensate the parasympathetic impairment.

Julius et al. hypothesized that the dominating sympathetic activity to compensate the parasympathetic impairment tends to decrease with time at the early stage of hypertension. This can also be a reason for the lack of significance in components of LF and HF. Julius et al. also hypothesized that the prolonged hypertension, dominating sympathetic activity, decrease in parasympathetic activity will lead to normal cardiac output, increase in vascular resistance and parasympathetic tone and decrease in sympathetic tone.(10)

Our study indicates that patients with hypertension are at higher risk as it shows decreased HRV levels and lower parasympathetic activity. Impaired heart rate variability predisposes the individual to increased risk for cardiovascular problems. Therefore early assessment of autonomic nerve function is advised in these groups. Observations in the present study have important implications to develop risk reduction strategies in order to reduce cardiovascular morbidity and mortality.

Limitations And Future Scope Of The Study

Some of the limitations of current study include:

- 1) The gender distribution in each group was uneven with female predominance in both groups
- 2) Moreover, the entire sample was selected from a single institution. This could limit the extrapolation of results to general population.
- 2) Not all HRV parameters were assessed in this study.
- 3) We used five minute HRV that reveals only short term changes in cardiac autonomic status and 24 h HRV is required to further consolidate the results.

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