DOI: 10.14260/jemds/2014/2646

ORIGINAL ARTICLE

HEART RATE VARIABILITY IN TYPE 2 DIABETICS WITH CHANGE IN POSTURE

V. Pramodh[1], Ashwini K. Shetty[2], M. Prashanth Kumar[3], B. A. Krishna Prasad[4]

HOW TO CITE THIS ARTICLE:
V. Pramodh, Ashwini K. Shetty, M. Prashanth Kumar, B. A. Krishna Prasad. "Heart Rate Variability in Type 2 Diabetics with Change in Posture". Journal of Evolution of Medical and Dental Sciences 2014; Vol. 3, Issue 21, May 26; Page: 5669-5676, DOI: 10.14260/jemds/2014/2646

ABSTRACT: AIM: To assess ability of cardiac autonomic function to cope with the physiological challenge of standing in Type 2 Diabetics. **METHODS:** This study was conducted in 40 normal and 40 Type 2 Diabetics, using short term Heart Rate variability test. **RESULTS:** The change in HRV values between the two postures were significantly reduced in Diabetics. ΔSDNN; Δ RMSSD, ΔNN50; ΔpNN50; Δ LF; Δ HF; Δ LF/HF ($p<0.05$) compared to healthy controls. **CONCLUSION:** This study demonstrates the presence of subclinical cardiac autonomic dysfunction in asymptomatic diabetics. More prospective studies on a large scale are required to validate this inference.
KEYWORDS: Heart Rate Variability (HRV), Diabetics, cardiac autonomic dysfunction.

INTRODUCTION: In 2013, according to International Diabetes Federation, an estimated 381 million people had diabetes. Its incidence is increasing rapidly, and by 2030, this number is estimated to almost double.[1]

Projections for the whole of India were 62.4 million people with diabetes in 2011 and 77.2 million people with prediabetes.[2]

It is known that the diabetics with cardiac autonomic dysfunction have higher incidence of fatal and non-fatal myocardial infarction. Cardiac Autonomic Neuropathy (CAN) is associated severe orthostasis, exercise intolerance, postural hypotension, enhanced intraoperative instability and an increased incidence of silent myocardial infarction (MI) and ischemia. Diabetic CAN, is associated with increased silent myocardial ischemia and mortality. It may even predict the development of stroke and hence has a poor prognosis.[3]

In the Detection of Ischemia in Asymptomatic Diabetics (DIAD) study of 1, 123 patients with type2 diabetes, CAN was a strong predictor of silent ischemia and subsequent cardiovascular events.[4]

HRV evaluation is a simple and reliable test that reflects autonomic regulation of heart rate. In the present study, we conducted the HRV test, in asymptomatic diabetics and their healthy controls.

MATERIALS AND METHODS: Ethical clearance for the study was obtained from the institutional ethical committee.

Study design: 35 Type 2 Diabetic males were enrolled in the study from a Medical college, in Bangalore rural district.

Similarly, 35 healthy male control subjects from the hospital attendants of patients (ward boys and male nurses, not related to patients) at a Medical College, Bangalore rural district were included in the study.

These study and control subjects were chosen based on the following Inclusion and Exclusion criteria.

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STUDY GROUP:

Inclusion Criteria:

1. Age: 55 -60 years.
2. Resting heart rate: 66-76 beats per min.

Exclusion Criteria:

1. Hypertensive.
2. Smokers and / alcoholics.
3. Cardiac complications (arrhythmias, history of Myocardial Infarction)
4. Nephropathy (serum creatinine> 2mg/dl)
5. Endocrine disorders (thyroid, adrenal etc.)
6. Those with injuries and painful conditi0ns such as arthritis.
7. Epileptics
8. Psychiatric disorders (depression, manic depressive illness etc.)
9. Treatment with drugs like antidepressants, B blockers, antiarrhythmic, ACE inhibitors, thyroid stimulants, anti-thyroid drugs.
10. Symptomatic diabetic autonomic neuropathy.
11. Trained athletes.

CONTROL GROUP:

Inclusion Criteria:

1. Age: 55 -60 years.
2. Resting heart rate: 66-76 beats per min.

Exclusion Criteria:

1. Hypertensive.
2. Diabetics.
3. Smokers and / alcoholics.
4. Cardiac complications (arrhythmias, history of Myocardial Infarction)
5. Nephropathy (serum creatinine> 2mg/dl)
6. Endocrine disorders (thyroid, adrenal etc.)
7. Those with injuries and painful conditi0ns such as arthritis.
8. Epileptics
9. Psychiatric disorders (depression, manic depressive illness etc.)
10. Treatment with drugs like antidepressants, B blockers, antiarrhythmic, ACE inhibitors, thyroid stimulants, anti-thyroid drugs.
11. Symptomatic diabetic autonomic neuropathy.
12. Trained athletes.

METHODOLOGY: The procedure of the HRV test was explained to the subjects in their own language and a well-informed written consent was taken. The HRV of the subjects was assessed 2 hours after food and without any caffeinated drinks or strenuous exercise meanwhile. Anthropometric measurements such as height (m), weight (kg) were recorded. Resting blood pressure was measured using a mercury sphygmomanometer. Resting heart rate was recorded.

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The resting ECG of 5 minutes was recorded in supine posture for all subjects, in lead II, in a state of physical and mental rest in a quiet, adequately illuminated and well ventilated lab. Then the subjects are asked to stand smoothly and further 5 minutes of ECG is recorded in the standing posture.

Similarly, the ECG of 5 minutes in supine and 5 minutes in standing postures was recorded in the control subjects.

The HRV equipment used was: RMS, VAGUS.MODEL: HRV. Serial no: HRV/121001/AOBX.

The following HRV parameters were recorded in each subject.

SDNN: Standard Deviation of the Normal to Normal beat R-R interval.

RMSSD: Root Mean Square of the Standard Deviations of the Normal to Normal beat.

R-R intervals.

NN50: Number of Successive Normal to Normal beat R-R intervals> 50 milliseconds.

pNN50: Proportion of Normal to Normal beat R-R intervals> 50 milliseconds out of total Normal to Normal beat R-R intervals.

VLF: Very Low Frequency (<0.04Hz): physiological significance unclear yet

LF: Low Frequency (0.04 – 0.1 Hz): reflects both sympathetic as well parasympathetic tone.

H: High Frequency (0.15-0.4): Mainly depicts the parasympathetic component.

For each frequency band, measurements from the PSD Estimate consisted of both absolute and relative power of VLF, LF, and HF bands.

LF and HF power bands were normalized

LF / HF: depicts the sympatho- vagal balance.

In short-term HRV recordings, Frequency domain methods are preferred to the time domain methods. The duration of recording should be at least for 10 times the lower frequency component wavelength. Thus, to assess the HF components of HRV, a recording of approximately 1 minute is required and approximately 2 minutes for assessing the LF component.[5]

The VLF, LF, and HF power components are measured usually in absolute values of power (milliseconds squared). LF and HF can be measured in normalized units (n.u) as well. The relative value of each power component in proportion to the total power minus the VLF component can thus be represented. The effect of the changes in total power on the values of LF and HF components is minimized by normalization. Measurements of LF and HF in normalized units (n.u) signifies the sympatho-vagal balance[5]

STATISTICAL ANALYSIS: Student t Test (unpaired T test) was used for the statistical analysis of the results obtained. This test was applied to compare the two sets of differences (Δ values for each parameter), between diabetic and non-diabetic due to change in posture in their respective groups, as depicted in figure1 for Δ SDNN and Δ LF/HF. Software used statistical analysis was: Open Epi. All the HRV indices were found to be of statistical significance between diabetics and healthy controls.

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RESULTS:

	Diabetics Supine (35)	Diabetics Standing (35)	Controls Supine (35)	Controls Standing (35)	Significance
SDNN	48.33±12.51	41.48± 11.37	64.19±21.41	52.17 ±18.84	p<0.05
RMSSD	27.02± 18.31	24.49 ±11.25	37.28 ± 14.94	44.31 ± 16.52	p<0.01
NN50	7.42 ± 1.04	5.08 ± 2.81	14.44 ± 3.03	10.37 ± 2. 2.4	p<0.01
pNN50	11.21± 2.44	8.27 ± 2.05	28.77 ± 4.14	17.81 ± 3.04	p<0.01

Table 1: Time Domain Parameters

	Diabetics Supine(35)	Diabetics Standing(35)	Controls Supine(35)	Controls Standing(35)	Significance
LF (n.u)	64.21±12.48	68.±10.21	60.78±9.49	69.15±27.82	p<0.05
HF(n.u)	33.29±12.51	30.28±14.1	39.37± 10.88	28.01±5.49	p<0.01
LF/HF	4.3 ± 1.3	4.8±2.3	1.7 ± 0.71	2.9 ±1.2	p<0.01

Table 2: Frequency Domain Parameters

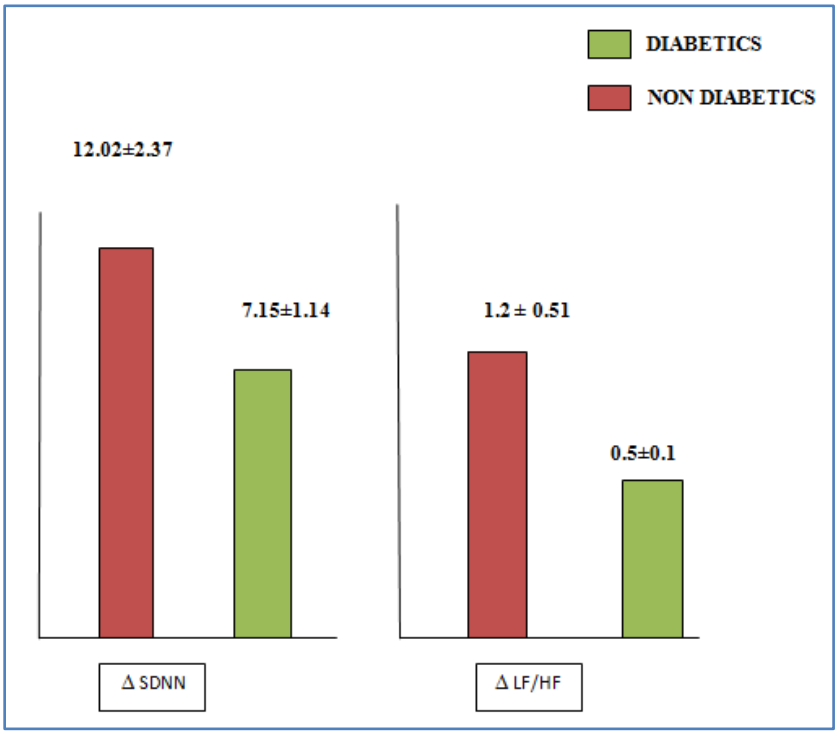

Fig. 1: Comparison of changes in SDNN and LF/HF values in Diabetics and Non Diabetics

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DISCUSSION: Heart rate variability is oscillation in the intervals between consecutive heart beats. Time domain" or "frequency domain methods of measuring the variation in HRV are used. These techniques are complementary to each other. Time domain measures are the standard deviation of normal R-R intervals (SDNN), the root mean square of successive R-R interval differences (RMSSD), and, the number (NN50) and percentage of normal R-R intervals that differ by >50 ms (pNN50). These are measures of HRV reflect specific physiological autonomic regulatory activities. The total power is denoted by SDNN but, both RMSSD and pNN50, which detect oscillations of high frequency, reflect the parasympathetic tone. Parasympathetic blockade reduces all HRV measures significantly.

LF and HF can be measured in normalized units (n.u) as well. The relative value of each power component in proportion to the total power minus the VLF component can thus be represented. The effect of the changes in total power on the values of LF and HF components can be minimized by normalization. Measurements of LF and HF in normalized units (n.u) reflect the sympatho-vagal balance. The HF component is thought to reflect the respiration induced modulation of vagus nerve discharge. The LF and VLF components reflect the variation in R-R interval influenced by more gradual co-ordination between sympathetic and parasympathetic systems.

Sympathovagal balance is reflected in the ratio of absolute LF to HF power. LF and LF/HF power are increased and time domain measures of HRV are decreased in upright tilt, due to an increased sympathetic tone. Beta-blockade is known to blunt these changes.[6]

In a meta-analysis of 12 published studies, Vinik et al reported a consistent association between CAN and the presence of silent myocardial ischemia, measured by exercise stress testing.[7]

In our study, we have observed that the SDNN values in Diabetics, signifying the total HRV, was significantly reduced ($p<0.01$) as compared to that of the controls. This can be attributed to the reduction in the indices signifying the parasympathetic tone such as the RMSSD, $P<0.01$); NN50, $p<0.01$); pNN50 ($p<0.01$). This is in concurrence with some of the earlier studies that have shown that there is a decrease in parasympathetic discharge even at rest in the study group. The changes in HRV values with change in posture were significantly reduced in Diabetics. We also found that Diabetics had increased LF/HF ($p<0.01$) signifying altered sympathovagal balance. This might also be due to increased sympathetic tone as reflected by increased LF ($p<0.05$). This results in a significant decrease in the ability to cope with the physiological challenge of standing.

An increased LF (expressed in normalized units) is observed by Malliani A et al during 90° tilt, reflecting an increased sympathetic tone. Similar changes were noted during mental stress, standing, physical activity and moderate exercise in healthy subjects, and also during moderate hypotension and physical activity.[8]

Malpas SC et al have found that HRV was significantly reduced diabetic subjects compared with the control group.[9]

It is reported that all the diabetes mellitus groups especially the diabetic neuropathy (DN) group, had lower time domain indices and nonlinear dynamics indices than a normal control group. R-R interval Poincare plots of the control group was of comet-shaped pattern, the uncomplicated diabetes mellitus group was mainly of torpedo-shaped pattern, while the DN group had more irregular patterns.[10]

Depressed HRV on 24-hour ambulatory electrocardiography monitoring is an independent risk factor for a poor prognosis in patients with CHF. Ponikowski P et al say that analysis of HRV could be recommended in the risk stratification for better management of patients with CHF after

further investigation.[11] Our study of the short term HRV of 5 minutes in diabetics is also effective in demonstrating the cardiac autonomic dysfunction in asymptomatic diabetics as the other long term (24 hour holter monitor) studies.[3] In one of the studies, it was found that diabetic patients with and without diabetic neuropathy had significantly decreased time-domain parameters (SDRR, SDRR index, SNN50, pNN50%, RMSSD and George index) compared to normal controls.[12]

La Rovere MT et al have stated that sudden death in patients with CHF can be precisely predicted by reduced short-term LFP during controlled breathing and that it is independent of many other variables. These findings are effective in identification of patients who may benefit from prophylactic implantation of a cardiac defibrillator.[13]

However, it is reported that change in LF/HF in diabetics to upright position was similar to changes in cardiac autonomic control in subjects with and without CAD. This suggests that though a normal response to changes in body posture and habitual physical exercise in patients with CAD, there is a derangement in autonomic responses to changes in central stimuli[14]

Andrew J.M et al, in their meta-analysis study demonstrated that risk of silent myocardial ischemia and mortality was very high in those with reduced cardiovascular autonomic function, as measured by heart rate variability (HRV).[15]

The association between silent ischemia and CAN has important implications, as reduced appreciation for ischemic pain impairs timely recognition of myocardial ischemia or infarction, hence delays appropriate therapy.[16]

Heart rate variability pattern study has the potential for detection of autonomic imbalance in the subclinical and asymptomatic stages. Glycemic Variability (GV) may affect the sympathovagal balance by increasing oxidative stress and proinflammatory cytokines. Therefore establishing a GV risk profile could be important in determining risk factors in diabetes patients.[17]

Measurement of HRV at the time of diagnosis of type 2 serves to establish a baseline, with which 1-year interval tests can be compared. Regular HRV testing provides early detection of early autonomic dysfunction and thereby promotes timely diagnostic and. Knowledge can encourage patient and physician. Therapeutic interventions to improve metabolic control can be effective for patients with CAN.[18]

Thus short term HRV test could be used as a screening tool for early detection of cardiac autonomic dysfunction at the diabetes clinics. Further studies to validate these inferences in large diabetic populations are required.

CONCLUSION:

1. Subclinical cardiac autonomic neuropathy is possibly prevalent in diabetic individuals as demonstrated by short term HRV tests.
2. Reduced ability of asymptomatic diabetics, due to cardiac autonomic neuropathy, to cope with a physiological orthostatic challenge as compared to healthy controls.

Early lifestyle changes and medical intervention can be instituted to attenuate the deterioration of autonomic functions.

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DOI: 10.14260/jemds/2014/2646

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AUTHORS:

1. V. Pramodh
2. Ashwini K. Shetty
3. M. Prashanth Kumar
4. B. A. Krishna Prasad

PARTICULARS OF CONTRIBUTORS:

1. Associate Professor, Department of Physiology, M.V.J.M.C & R.H, Hoskote, Bangalore.
2. Assistant Professor, Department of Physiology, M.V.J.M.C & R.H, Hoskote, Bangalore.
3. Professor, Department of Physiology, M.V.J.M.C & R.H, Hoskote, Bangalore.
4. Professor, Department of Physiology, M.V.J.M.C & R.H, Hoskote, Bangalore.

NAME ADDRESS EMAIL ID OF THE CORRESPONDING AUTHOR:

Dr. V. Pramodh,
Associate Professor,
M.V.J.M.C & R.H, Hoskote,
Bangalore.
Email: drvpramodh@gmail.com

Date of Submission: 03/05/2014.
Date of Peer Review: 05/05/2014.
Date of Acceptance: 15/05/2014.
Date of Publishing: 20/05/2014.